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The iPhone, Cracked Open p30

Can a Pill Extend Life?

Ellen Swallow Richards DM12



technology review

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So who's holding whom over a barrel?



Contents

Volume 110, Number 5



Cover illustration by Oliver Hibert

7 Contributors

- 8 Letters
- 10 From the Editor

Forward

19 Mapping Censorship

When it comes to Internet censorship, China and Iran top the list

20 Shopping Search

A cell-phone service guides users to nearby bargains—sometimes

20 Portable Hurricane

Machine will help Florida update its building codes for storms

21 Nano Curry

Encased curcumin could be a drug

21 **Seeing Signs of Diabetes**Molecular tracers spot the disease

22 **Silicon-Based Spintronics** First-of-its-kind computing prototype

22 Self-Healing Plastic

A material repairs itself multiple times

24 Wireless Recharging

MIT researchers send power two meters with no wires

24 Invisible Ink from Xerox

Cartridge works in standard printers

26 Featured Startup: Vlingo

Company's voice-recognition interface unlocks the mobile Web *And more ...*

Features

47 The TR35

Technology Review presents its seventh class of outstanding innovators under the age of 35. These driven, creative people will alter the state of medicine, computing, communications, and energy. Their work represents the future of technology.

78 The Enthusiast

A controversial biologist at Harvard claims he can extend life span and treat diseases of aging. He just may be right. **By David Ewing Duncan**

84 Essay: Letter to a Young Scientist

In this excerpt from his newly released memoir, the famous biologist tells of his role in determining the structure of DNA. By James Watson

Hack

30 The iPhone

Apple's phone sets a new standard, but not with wholly unique hardware. By Daniel Turner

Q&A

32 Alieu Conteh

How an African entrepreneur put cell phones in Congo By Jason Pontin

Notebooks

36 Protecting Security and Privacy

The ubiquitous computational devices of tomorrow will pose risks. By Tadayoshi Kohno

36 The Future of Manufacturing

Self-assembly is the key to building complex nano devices. By Babak A. Parviz

37 Cells by Design

What synthetic biology most needs is a better way to synthesize DNA. By J. Christopher Anderson

Photo Essay

38 Body Parts, New and Improved

Amputee athletes are getting faster and stronger.

By Emily Singer

Reviews

98 Higher Games

It's been 10 years since IBM's Deep Blue beat Garry Kasparov in chess. What did the match mean? By Daniel C. Dennett

100 Electric Cars 2.0

Plug-in hybrids could bring gas-free commutes. But will they get made? By Kevin Bullis

102 Patent Law Gets Saner

The U.S. Supreme Court has sent a clear message to "patent trolls." By Scott Feldmann

Demo

104 Illuminating Silicon

Optical devices made of silicon could transform communications networks and computing.

By Kate Greene

From the Labs

- 108 Nanotechnology
- 109 Biotechnology
- 110 Information Technology

5 Years Ago in TR

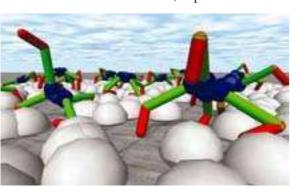
112 Please Don't Give Me a Break!

Catching up with Max Levchin By Michael Patrick Gibson

What's New on Our Website

technologyreview.com/tr35

Learn more about the TR35 honorees on our website. See Josh Bongard's robots explore new terrain in computer simulations (p. 74), or toy with a virtual nanogenerator based on Xudong Wang's research (p. 72). You'll also find mini-documentaries about the TR35 Innovator of the Year, David Berry, and Humanitarian of the Year, Tapan Parikh.



technologyreview.com/prostheses

This issue of the magazine features a beautiful photo essay on amputee athletes who use a range of new, sophisticated prostheses (p. 38). Online, you'll find video of the athletes in action. See Rudy Garcia-Tolson cycle using a prosthetic knee, and watch Hugh Herr easily attach, adjust, and walk on his powered ankle.

technologyreview.com/sirtuins

This issue features a profile of David Sinclair, a controversial Harvard biologist who is testing drugs to fight aging (p. 78). Online, we've posted an explanation of the science behind antiaging genes and how a new class of compounds might activate them. Written by Sinclair and several of his colleagues, including Leonard Guarente, the MIT molecu-

lar biologist who discovered the antiaging gene *sir2* more than a decade ago, and Christoph Westphal, CEO and cofounder (with Sinclair) of Sirtris Pharmaceuticals, the article is an excellent technical introduction to this exciting field of research.



technologyreview.com/iphone

This month, *Technology Review* takes the Apple iPhone apart and explains what's inside (p. 30). Check out our website for an animated look at the phone's hardware.



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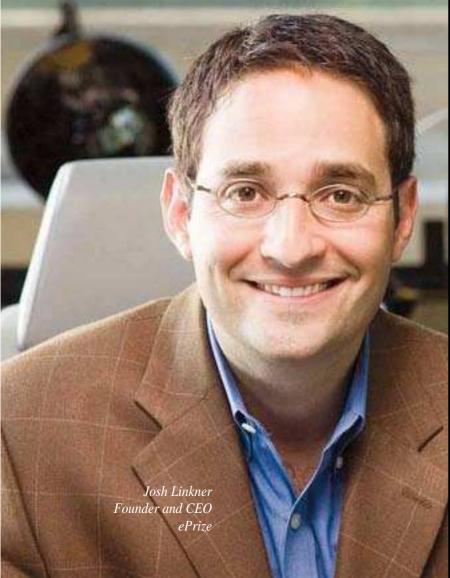
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ePrize is the model for innovation and Internet success. Michigan helped them break the mold.









If you thought you needed a West Coast zip code to make it on the web, think again. Case in point: ePrize — a globally successful interactive promotion company that works with the world's top brands. Not only did ePrize find a great creative talent pool here with some of the best colleges and universities on the planet, they also found a great place to call home in Pleasant Ridge, Michigan. Hot clubs, great restaurants, year-round sports and recreation, friendly tree-lined neighborhoods and a world-class arts community.

ePrize also found financial and economic incentives from the Michigan Economic Development Corporation to put their Internet business out in front. As Josh Linkner, founder and CEO of ePrize, put it..."All the production, all the technology, all the innovation, is happening right here in Michigan."

So is it time to move your entrepreneurial company to Michigan? Absolutely. And we'll do whatever it takes to make that happen. Because wherever on the web you compete, Michigan can give you the upper hand. Let the Michigan Economic Development Corporation show you how to break the mold. Click on michigan.org/upperhand.



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TECHNOLOGY REVIEW READER:

MARY FINLAY

DEPUTY CHIEF INFORMATION OFFICER, PARTNERS HEALTHCARE SYSTEM

Mary is responsible for managing the 1,300 IT and telecom professionals who support Partners Health-care, a huge institution comprising 10 hospitals and facilities in the Boston area—including two of the nation's finest hospitals, Massachusetts General and Brigham and Women's. She says wants to "bring the best technology to our physicians so that they've got the information they need, and sophisticated support for the clinical systems upon which they depend." *Technology Review* is the magazine she reads to learn which emerging technologies will help her do her job better: "I love *Technology Review* because it really looks to the future."



James Watson was awarded a Nobel Prize in 1962 for his part in discovering the double-helical structure of DNA—a story recounted here

("Letter to a Young Scientist," p. 84) in an excerpt from his new book, Avoid Boring People: And Other Lessons from a Life in Science. The book, says, Watson, "is my autobiographical romp through academia, including lessons learned that have helped keep me, at 79, more alive than dead." Watson is the author of Molecular Biology of the Gene and The Double Helix. He is now chancellor of the Cold Spring Harbor Laboratory.

Daniel C. Dennett is a philosopher who has long argued that artificial intelligence might one day produce machines that can be said to be conscious. In this issue, he discusses AI



and chess: it was 10 years ago that Deep Blue beat world champion Garry Kasparov ("Higher Games," p. 98).

"We're a long way

from human-level AI," says Dennett, "but the 'philosophical' arguments against achieving this are all bogus. Could we design and build a robotic bird that could catch insects on the fly and land safely on a twig? It would be an incredibly difficult tour de force of engineering, but not 'impossible in principle.' The same goes for human-level AI. We may never achieve it, but only because it will be too expensive and frivolous to try. We can learn what we need to know by building simpler models."

Dennett is the author of *Consciousness Explained*, *Darwin's Dangerous Idea*, and *Breaking the Spell*. At Tufts University, he is a University Professor and codirector of the Center for Cognitive Studies.

Stephen S. Hall, for this year's TR55 package, profiled David Berry, our Innovator of the Year (p. 48). Though Berry, a Harvard-trained MD, has done a few different things since earning his bachelor's degree from MIT in 2000—he developed a treatment for stroke and worked on a new approach to cancer therapy—he is now



concentrating, in his work at Flagship Ventures, on genetically engineering microbes to produce biofuels. His ideas are at the heart of

Flagship-backed LS9, a Californina-based renewable-petroleum company. "I was impressed by David," Hall says. "He conveys a very low-key form of energy and high-minded restlessness, yet the breadth of his interests is unusually wide. While he was still attending medical school at Harvard, he organized a fairly high-powered roundtable at MIT on alternative fuel technologies. That says a lot about how broadly he approaches innovation."

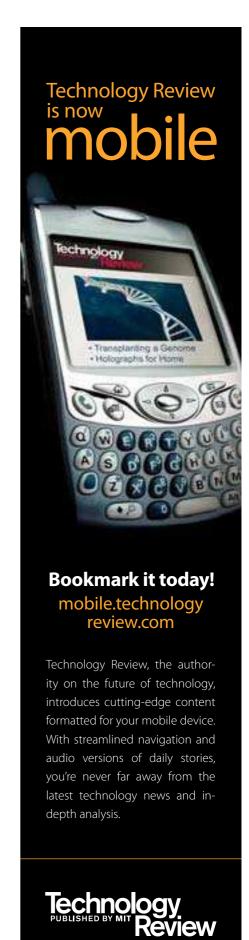
Hall is the author of five books about contemporary science. His most recent, *Size Matters*, was published last year and examines the disadvantages of being short. Hall writes frequently for the *New York Times Magazine*, *National Geographic*, and a number of other magazines.

Oliver Hibert illustrated this issue's cover. "I had a fun time designing this," he reports. "Listening to music



is an essential part of the way I design, and the music of choice for this project was '60s psychedelia and '80s electro-pop. Good

times." Hibert works in many media, but painting is his chief love. He has had shows in museums and galleries around the world, and he currently lives in Phoenix, AZ.



Letters

Second Life

I've been following the virtual world called Second Life for some time, so it was a pleasure to read Wade Roush's thoughtful and intelligent cover story ("Second Earth," July/August 2007). The piece benefited greatly from the fact that your writer entered into the life of the community he was trying to understand.

I'm sure you'll receive some splenetic, sarcastic criticism of the piece from someone disgusted by the very idea of a Second Life. Unlike Roush, though, your critic will almost certainly have spent no time in acquiring one.

Michael Parsons Editor, CNET.co.uk London, England

Artificial Intelligence

In his essay arguing against the possibility of producing conscious machines ("Artificial Intelligence Is Lost in the Woods," July/August 2007), is Yale computer science professor David Gelernter arguing against artificial intelligence or artificial humanity? Intelligence does not require all the human interactions with the world or emotions that he lists, unless there is a particular need to provide those for the intended application.

Consciousness is hard to define. Maybe someone should make a replacement for the Turing test, Alan Turing's suggestion that if a computer can answer questions the same way a human would, then it can be considered intelligent. A Helen Keller test, perhaps: it may be possible, after all, that there is or will be a computer in existence that is conscious, but for

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whom we have not provided the means for input or output that it would need to signal to us that it is conscious. Or maybe it's speaking "Chinese" to an "English" world or broadcasting radio to a television world.

I think we'd better find a more general concept of consciousness than Gelernter's so that, at a minimum, we'll recognize that aliens have landed if they ever do.

Stanley D. Young Fort Collins, CO

I side with the anticognitivists (and thus David Gelernter). AI software running on von Neumann machines will never be conscious, and without consciousness there can be no experience, human or otherwise. Believing that somehow consciousness will arise like a deus ex machina on your Pentium is an article of religious faith.

Still, while AI software cannot replicate consciousness, networks of artificial neurons have considerably more promise. Consider machines being built by Kwabena Boahen's group at Stanford or earlier by Carver Mead's student Misha Mahowald at Caltech.

There are also hybrids in which real neural circuits are emulated in very large-scale integration (VLSI): Paul Rhodes's group at Evolved Machines in Palo Alto is working on that, as is Theodore Berger's group at the University of Southern California.

Digital computers are so second millennium. As my MIT classmate Ray Kurzweil might say, "Plug that silicon retina into your optic nerve, and you won't know the difference."

Robert Blum Menlo Park, CA

Good Design

Your design-focused May/June 2007 issue was very interesting and thought-provoking, but I think it missed an opportunity to focus attention on the most pervasive problems of electronic-product design.

Several experts and writers equated operational simplicity with minimal functions, and several cited the iPod as an example of gaining simplicity by avoiding feature creep. But the history of the iPod is feature creep itself. It started out as a music player. Now it plays music, podcasts, video, and games; it can act as a stopwatch or alarm clock, show you the time in other world cities, maintain your contacts and calendar, show photos, allow you to read text files, and serve as a backup hard drive. Why does it remain simple to use? Because all the functions work the same way. The user needs to learn only one rule about the interface and can apply it to every function on the device.

Victor Riley
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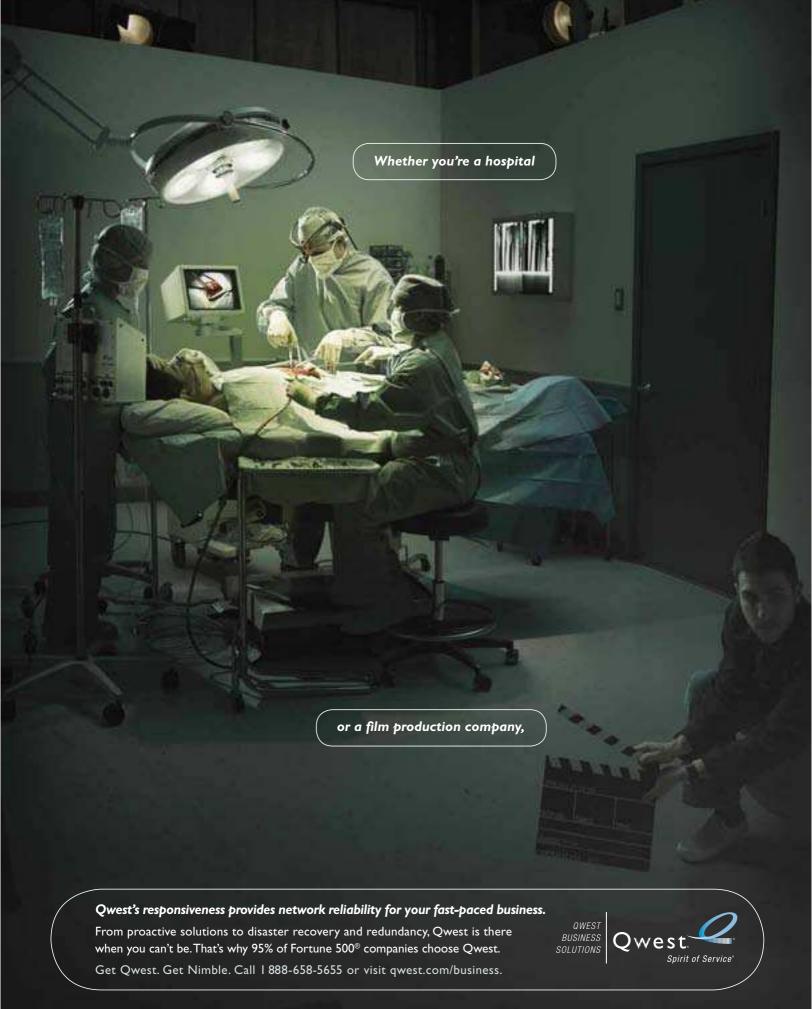
Changing Human Nature

I read with interest the essay by philosopher Roger Scruton ("The Trouble with Knowledge," May/June 2007), since I enjoy seeing things in new ways and respect philosophers for their penetrating insight and clear logic. But I found neither in Scruton's piece.

Scruton fears that future technology will enable men and machines to interact in increasingly intimate ways and eventually merge to the degree that human nature itself is altered. He is terrified of this possibility.

But what, exactly, is so great about human nature that he is so scared of its changing? One need only read a newspaper to see, not only that human nature is deeply flawed, but also that it is human nature not to need a reason to believe something that makes you feel good; it is human nature to believe whatever superstitions you were taught as a child. Scruton certainly seems to. When he starts to mention God, and refers to the Fall of Adam, I suspect that nobody is going to get much of a clear and rational discussion from him.

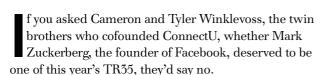
Don Dilworth
East Boothbay, ME



From the Editor

Whom Should We Reward?

Innovations in technology and science have many authors, although only a few are recognized



We named Zuckerberg (p. 65) one of 2007's 35 leading innovators under the age of 35 because Facebook is the best of the social-networking websites, and social networking is the fastest-growing phenomenon on the Internet. As of July 2007, 30 million people had registered with Facebook. An older social network, MySpace, has more than 100 million people registered, but Facebook is cooler. Its design (for which Zuckerberg is responsible) is more elegant and functional, and its features are more useful and more fun. To the young and hip, Facebook appears to enjoy the future's blessing, but MySpace already looks dated and ugly.

This perceived coolness has real value, or soon will. Facebook is a private company, and its value is still notional, but last year Zuckerberg was widely reported to have declined an offer of \$1 billion from Yahoo. When Facebook enjoys its "liquidity event" (in the form of either acquisition or an initial public offering of stock), Mark Zuckerberg, who is 23, will be very rich.

But the Winklevoss brothers say that Facebook's founder stole the idea of the site from them. In a suit that dates back to 2004, the ConnectU founders accuse Zuckerberg of lifting their source code and business plan.

In 2002, when the Winklevoss brothers and Divya Narendra, another founder, were juniors at Harvard, they conceived what they initially called the Harvard Connection, a social network for the college. In November 2003, they asked Zuckerberg to develop the software, promising to compensate him later if the site prospered. Zuckerberg left the project in February 2004, a month after registering the domain name thefacebook.com. By the end of February, Zuckerberg's new site, also a social network for the Harvard community, had registered half the college's undergraduates. By April, the Facebook had expanded to other Ivy League schools. Later, it began to serve more universities, then high schools, then businesses, and eventually the broader public. By contrast, ConnectU never really got started. It didn't launch until May 2004; overshadowed by what soon became simply Facebook, today it boasts no more than 70,000 users.

Those bare but evocative facts are *all* that is undisputed in the case. The Winklevosses say their business plan always described how the Harvard Connection would



grow beyond the college and become ConnectU—just as Harvard's "the Facebook" became the world's Facebook. For his part, Zuckerberg says he never imagined that his unpaid arrangement was contractually binding.

The parties declined to be interviewed for this column. But I have no doubt that both the Winklevoss brothers and Zuckerberg are sincere in their expressions of outraged rectitude (although I am sure the twins' grief could be diminished by a large settlement). Both parties believe they created the idea of a well-made social network, constructed to please the tastes of clever college kids.

But in every case where a new technology or scientific idea is emerging, there will be many people working on it, and nearly as many claims to have originated it.

Some have argued, for example, that James Watson, who discovered the structure of DNA with Francis Crick, never properly acknowledged his inspiration for the idea that that structure was a double helix. Famously, Maurice Wilkins of King's College London showed Watson research that belonged to Rosalind Franklin, a chemist and crystallographer then working at King's, without her knowledge or permission. According to Watson, whose account can be found in this month's essay (see "Letter to a Young Scientist," p. 84), the x-ray photograph of DNA he saw "displayed unequivocally the large cross-shaped diffraction pattern to be expected from a helical molecule." That information, in part, led to the Nobel Prize that Watson shared with Crick and Wilkins in 1962.

In his essay, Watson discharges his debt to Franklin, writing that "we would not have found the DNA structure without knowledge of x-ray results from King's." He argues, however, that scientific and technological innovation occurs when competitive researchers and innovators, all avid for success, confront a problem separately. Each failure or advance contributes to the larger project. He's right, but it is a melancholy fact that while many may help develop a bright idea, our prizes, copyrights, patents, and financial markets recognize just a few.

Watson and Crick would not have discovered the structure of DNA without Franklin. Without ConnectU, Facebook almost certainly would not look as it does. In hindsight, and after rancorous controversy, we have come to better understand the contributions of Franklin and others at King's. In the case of Facebook, will a lawsuit clarify what is confused? Write and tell me what you think at jason.pontin@technologyreview.com. Jason Pontin





Solar Energy in Spain

Spain is forging ahead with plans to build concentrating solar power plants, establishing the country and Spanish companies as world leaders in the emerging field. At the same time, the number of installed photovoltaic systems is growing exponentially, and researchers continue to explore new ways to promote and improve solar power. This is the seventh in an eight-part series highlighting new technologies in Spain and is produced by Technology Review, Inc.'s custom-publishing division in partnership with the Trade Commission of Spain.

From the road to the Solúcar solar plant outside Seville, drivers can see what appear to be glowing white rays emanating from a tower, piercing the dry air, and alighting upon the upturned faces of the tilted mirror panels below. Appearances, though, are deceiving: those upturned mirrors are actually tracking the sun and radiating its energy onto a blindingly white square at the top of the tower, creating the equivalent of the power of 600 suns. That power is used to vaporize water into steam to power a turbine

This tower plant uses concentrating solar technology with a central receiver. It's the first commercial central-receiver system in the world.

Spanish companies and research centers are taking the lead in the recent revival of concentrating solar power (CSP), a type of solar thermal power; expanses of mirrors are being assembled around the country. At the same time, Spanish companies are investing in huge photovoltaic (PV) fields, as companies dramatically increase production of PV panels and investigate the next generation of this technology. Spain is already fourth in the world in its use of solar power, and second in Europe, with more than 120 megawatts in about 8,300 installations. Within only the past 10 years, the number of companies working in solar energy has leapt from a couple of dozen to a few hundred.

Power from the Sun's Heat

Southern Spain, a region known the world over for its abundant sun and scarce rain, provides an ideal landscape for solar thermal

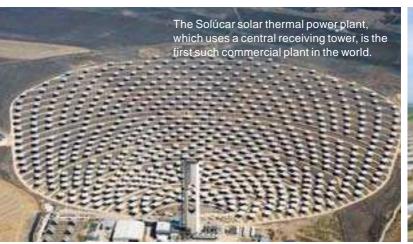
power. The tower outside Seville, built and operated by Solúcar, an Abengoa company, is the first of a number of solar thermal plants and will provide about 10 megawatts of power. The company Sener is completing Andasol 1, the first parabolic-trough plant in Europe—a 50-megawatt system outside Granada that will begin operation in the summer of 2008.

Unlike photovoltaic panels, which harness the movement of electrons between layers of a solar cell when the sun strikes the material, solar thermal power works by utilizing the heat of the sun. CSP has until recently cost nearly twice as much as traditional natural gas or coal power plants, and it is effective only on a large scale. "You need a very large budget to set up a concentrated solar power system," says Eduardo Zarza, director of concentrating solar research at the Solar Platform of Almería (PSA in Spanish), a research, development, and testing center. "You need a great deal of land, a steam turbine, an electricity generator, power equipment, people in the control room, staff to run the system." The costs are also front-loaded, unlike those of traditional plants: the fuel is free, unlike oil, gas, or coal, but the up-front development expense is significantly higher.

During and immediately following the energy crisis of the 1970s, nine solar thermal plants were built in California to produce a total of 350 megawatts, but until this year no new commercial plant had been built, anywhere in the world, for 15 years.

PV costs run nearly double those of solar thermal for a power plant of a similar size, but PV has the advantage of modularity; panels can be incorporated into individual homes, companies,







At this plant, we're working with the potential of about 3,000 suns—so it has to be very well designed and operated to provide the best results."

and buildings or installed in small spaces. This micropower approach has helped the market for PV explode in the past five years, while solar thermal remained moribund.

With gas costs rising and the world sharpening its focus on global warming, and governments around the world making a concerted attempt to invest in alternative energy sources on a larger scale, solar thermal is attracting new attention. In Spain in particular, the technology has been assisted by Royal Decree 436, implemented in March 2004, which approved a feed-in tariff (a guaranteed price) for solar thermal power. The feedin tariff made building this type of power plant economically viable. The government also recognizes that, as with wind, support is necessary at the beginning to enable the creation of new plants-which will most likely drive down prices, as has happened in Spain with wind power.

Technologies

The most common technology so far, and the one in use at Andasol 1, is based on a series of parabolic troughs, huge curved mirrors about 18 feet wide that collect the sun's energy and focus it on a receiver pipe in the middle. Oil streams through that pipe along a long loop of troughs. The mirrors slowly track the sun from east to west during daytime hours, and the oil reaches about 400 °C (about 750 °F).

The heat transfer fluid then travels to a steam generator, where the heat is transferred to water, immediately turning the water into steam. That steam powers a turbine, the same technology used in conventional power plants.

The tower technology works on the same principle as the troughs—the sun's heat—but uses curved mirrors called heliostats, mounted on trackers that shift position with a slight mechanical groan every few seconds. The heliostats direct the sun's light to a central receiver at the top of the tower. Testing towers have been built in Spain, the United States, and Israel, but the Solúcar PS10 site is the first commercial application of the technology.

At PS10, 624 heliostats, 120 square meters each (nearly 1,300 square feet), concentrate solar radiation at the top of a 115-meter tower (about 377 feet). A receiver at the top transfers the heat directly to water, and the pressurized steam reaches 250 °C.

The engineering behind such a plant takes into account both the need to heat up the receiver and the importance of moderating the energy directed at it. "At this plant, we're working with the potential of about 3,000 suns, but the absorption panels can only handle 600 suns," says Valerio Fernández, head of engineering and commissioning for Solúcar. "We have to control the aiming to protect the solar panels. So it has to be very

well designed and operated to provide the best results."

Fernández says that so far the facility is operating as intended, but improvements will be incorporated into future towers. "This isn't the best temperature for the highest efficiency," he says, "but we wanted to test the safety and security of the design for this first installation. We'll do the remaining research necessary in order to use higher temperatures in future plants." He explains that the cooling system for the boiler is more complicated as temperatures increase, but that once those changes are implemented, the tower's efficiency could improve by 20 percent.

The tower is also supported by a small amount of natural gas, used when a stretch of rainy or overcast weather prevents the plant's full operation and the stored energy cannot stretch far enough to compensate. "It's good to be able to maintain stability, not be stopping and starting up the turbines more than once a day, as they're designed to do," says Fernández.

When completed in 2012, the entire Solúcar facility, called the Sanlúcar La Mayor Solar Platform, will generate more than 300 megawatts of solar power, using tower and trough technologies along with PV installations. Abengoa, owner of Solúcar, has also recently signed plans to build combined-cycle power plants in Algeria and Morocco, using parabolic



troughs in conjunction with natural-gas power plants.

One of the main advantages of solar thermal power, in addition to the cost benefit, is the potential for power storage. The Solúcar tower uses a system of heat storage based on pressurized water. Sener's Andasol site will use a more advanced system taking advantage of the specific properties of molten salt. It's been tested in Spain but has not yet been implemented commercially.

Located about an hour outside Granada, home to the world-famous Alhambra, Andasol 1 will provide power well into the evening hours. Sener, which is constructing the plant with a company called Cobra, has built extra troughs that will direct heated oil to 28,000 tons of molten salt (the salt is being imported from Chile). The salt must reach a high enough temperature to liquefy—and then it must be maintained in a liquid state to prevent it from causing blockages. Tubes carrying heated oil will pass through the molten salt, raising the temperature even higher, and the salt will retain the heat energy. As evening falls, the thermal energy will be transferred back to the oil, which will continue on to the heat exchanger and power the steam turbine.

One of Sener's innovations in this field was the development of new simulation software, called Sensol, that takes into account all the variables that go into building a solar plant, determining the production costs and the appropriate dimensions. This technology has also been used outside the country; the Japa-

nese Institute of Technology purchased Sener's services to determine the best dimensions for a solar plant it wanted to develop.

Andasol is Sener's first solar thermal site, though the company has already broken ground on another site nearby, and a third is being planned for a location in the northern part of country.

The company has faced hurdles in building this facility, the first major parabolic-trough system in Spain. "There have been a lot of challenges," says Nora Castañeda, an engineer in charge of the site's construction, laughing. "We can begin with the design itself. It was difficult to find the right manufacturers, because there are so few suppliers of the parts. We had to learn how to assemble a solar field like this in a short time. Once we solved one problem, another appeared."

But as quickly as problems have appeared, she says, the staff worked hard to find solutions. They built an assembly plant on-site and worked with Spanish construction companies to create appropriate jigs with laser trackers for the extremely precise task of building the parabolic mirrors and transporting the system to the field without disruption. Castañeda says she expects the lessons learned from Andasol 1 to help drive down the cost of future systems.

Other companies are part of this rising trend: the Spanish utility giant Iberdrola recently announced plans for 10

parabolic-trough systems across the country.

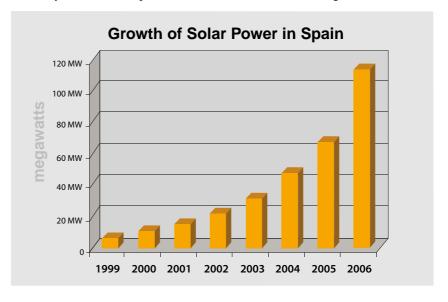
Advancing the Field

Eduardo Zarza is having a great day. In fact, he's having a great year. With a barely suppressed grin, PSA's director of concentrating solar research describes how the center has gone from a research outpost, where he and other researchers toiled away on solar thermal power for 25 years, to an international superstar (at least in certain circles), with near daily visits from companies and scientists from around the world.

Says Zarza, "Every week we have several companies coming to see the facilities to get information, because they're interested in investing in solar thermal plants. The situation has changed dramatically in only two years."

The center, surrounded by dusty rose-colored mountains dotted with green, lies in a particularly dry area, with only 20 percent of Andalusia's average rainfall. Back in the 1970s, with Western countries feeling the pressure of restricted access to oil, a consortium of nine countries—eight European nations and the United States—signed an agreement to investigate two solar technologies: one based on parabolic troughs, the other on a central receiver (like Solúcar's tower receiver).

In 1985, the test results were in: both technologies were commercially feasible, but costs were too high.



Since then, the center has continued testing and refining the technology, working with universities and countries around the world. Though there are other research centers with departments dedicated to concentrating solar power, PSA is the largest such research center in the world.

The center is one of two Spanish research facilities that operate as part of what's known as Ciemat (the other, near Madrid, focuses on wind and biomass). Sixty percent of the budget comes from the government, while the other 40 percent comes from grants and industry partnership. Lack of funds threatened the center's operations several times, and it nearly closed.

A rapidly growing interest in renewables, government incentives to promote energy alternatives, and the rising cost of oil and gas placed PSA in the perfect position to take a leading role in the development of renewable energy technologies. After decades in the literal and figurative desert, Zarza finds himself at the center of a renaissance: the technology is finally, once again, entering the marketplace—and the center's activities appear secure and are flourishing.

"We're very happy with the situation now," says Zarza. "In the past, few people wanted to learn about our systems—now, everybody wants to."

Research has focused on technologies to increase the efficiency and decrease the cost of these concentrating solar systems. Reflectors and absorber pipes have been refined, and the coupling between the solar and conventional systems has been improved. The use of molten salt for heat storage was tested on-site before Sener went ahead with plans to install such a system in the new Andasol facility. Researchers also continue partnering with European companies to develop alternative and even more effective storage systems, which could greatly increase solar thermal's viability in the marketplace.

The center is currently investigating replacing heating oil in absorber pipes with water, so the steam turbine could be linked to the solar field directly, bypassing a heat exchanger. "Conceptually, this seems so simple," says Zarza, "but that's not actually the case. Water boils and then turns to steam, and during the transition phase there could be very high temperature differences between the top and

bottom of the glass tube, which could cause it to break." Heating oil, unlike water, remains in liquid form throughout the process. Scientists have tinkered with tubes to develop one that can withstand these temperature changes, and soon a new three-megawatt facility will be built at PSA to test it.

Fernández of Abengoa's Solúcar, one of the companies participating in the research project, looks forward to replacing heating oil with water. "Oil is expensive," he says, "and in theory you can go to higher temperatures with water and pressurized steam, because oil has a heat limit. It's also more efficient if you can do away with the heat exchanger."

A significant challenge facing developers of CSP plants remains cost—in large part because these plants haven't been built before. Parabolic mirrors must be produced to exacting specifications, and tubes for the oil must be made of two glass layers with a vacuum between them. There's currently one mirror manufacturer in Europe and two manufacturers of the glass tubes, one in Israel and another in Germany. "So when there are more manufacturers producing those tubes, and when there's a larger production in general, you're going to get more competition and a scale advantage," says Peter Duprey, director of Acciona Energy North America, a subsidiary of a Spanish company. He adds, "I think this is at a fairly early stage in its evolution, and with more money and more people focusing on this energy alternative, I think you're going to drive costs down, just like what happened with wind. In the 1980s it was 30 cents per kilowatt-hour; now it's down to about 7 cents. I think you'll see the same thing with concentrating solar."

Both Abengoa and Sener are working with other Spanish companies to jump-start the production of parabolic mirrors and glass tubes in Spain, to increase production, competition, and local access to the necessary parts. At least two local companies will begin producing mirrors within the year, and another few are investigating developing new absorber pipes.

"Electricity costs are going up—and solar thermal costs are going down," says



Spanish companies continue to innovate in the technology and marketing of photovoltaic power.

S5



Zarza. "We think they will meet somewhere in the middle."

In the U.S.

The first solar thermal power plants in the world, nine in total, were built in Kramer Junction, in dry, sunny southern California, in the 1980s. They still harness 350 megawatts of solar heat. Since the last of those plants was built, however, the technology halted in the United States, as it did in the rest of the world. Research continued at American research centers such as the National Renewable Energy Lab (NREL).

This summer, the first new plant, built by Acciona with technology from the U.S. company Solargenix, came on-line outside Las Vegas in the abundantly sunny Nevada desert.

The Spanish company acquired 55 percent of Solargenix early in 2006 and then began plans to build Nevada Solar One, as the plant is known. The parabolic troughs supply 64 megawatts, enough to power about 14,000 homes annually. Acciona is also in the permitting stage for two 50-megawatt CSP plants in Spain.

Duprey, director of Acciona Energy North America, says, "In the southwest of the U.S. we have plenty of land that effectively is unused, and is near grid

Electricity costs are going up—and solar thermal costs are going down. We think they will meet somewhere in the middle."

connection points. That can be developed, and I think we can get gigawatts worth of concentrating solar power over the next 10 years."

Nevada requires its utilities to generate a percentage of their electricity from renewable sources. The wind is weak in southern Nevada, but the sun burns hot, and the state provided an investment tax credit—so Acciona took on the project.

This type of technology demands vast amounts of land for the parabolic troughs, and the plant is most efficient if it can be sited close to the demand. Conditions in the western United States, particularly the Southwest, meet both those requirements. The Western Governors' Association has stated its commitment to increasing the use of solar thermal power in the region.

Photovoltaics

The growth of solar in Spain is hardly limited to thermal power. Photovoltaic technology is still the primary source of solar power; it has been central to the solar-power repertoire since the 1970s, when

researcher Antonio Luque was sent to the United States to share information about microelectronics. He became inspired by American work on PV and returned to Spain, founded the Institute for Solar Research (IES in Spanish) in 1975, and eventually spun off the company Isofotón in 1981. By 1982 the company was already marketing the first Spanish solar cells.

Luque's first contribution to the solar field was the development of bifacial cells, which take advantage of sunlight from both sides. These cells provided Isofotón's start, but higher development and maintenance costs prevented their early adoption, and Isofotón reverted to conventional solar cells.

Today, the 60 researchers at IES—one of the oldest solar centers in the world—continue to push ahead with advances in PV technology. The institute's research areas include multijunction cells that utilize a wider bandwidth of solar energy; intermediate-band cells that can capture lower-energy photons; and concentrator systems in which lenses

multiply the sun's energy up to 1,000 times by focusing its light on tiny cells. The last technology is being developed in partnership with Isofotón.

To further develop this new technology, the Institute for Photovoltaic Systems of Concentration is being built in Puertollano, south of Madrid. Companies from Spain, including IES partner

which has been in Spain for more than 20 years and is now planning a major production expansion. In addition, the Spanish company Atersa builds solar panels and provides full solar-power installations. At its new Valencia factory, the company has grown to 14 megawatts of annual capacity and will soon expand to 30 megawatts. Another young solar panel company expe-

Outside the building, a panel of concentrating PV cells is mounted on a tracker. Unlike standard photovoltaics, which can accept all ambient light, concentrating PV cells are most efficient when tracking the sun to appropriately focus the light through the lenses. Thus, as with solar thermal, the technology will probably be most effective on a

Most of the energy increase in the world will be in electricity, and most of that will be in developing countries."

Guascor Fotón, will have demonstration sites, along with companies from the United States, Germany, and other countries. The goal is to improve the technology's efficiency and decrease its cost in an effort to speed commercialization.

Luque thinks solar cells will become much cheaper, but he acknowledges that a precipitous drop in price will require technological breakthroughs. He believes these breakthroughs might be occurring already and that the technological advances in store for PV will allow it to easily overtake solar thermal, even on a power-plant scale.

In a huge, airy, light-filled building near Málaga on Spain's southern coast, Luque's spinoff company, Isofotón, hums with the excitement of the exploding PV scene. This factory was completed in 2006, and ground has already been broken next door for an expansion.

The company's production and sales have shot up in the past few years, despite rough patches since its inception in 1981. Isofotón nearly went bankrupt twice as solar power languished worldwide. But in the late 1990s, Germany decided to invest heavily in solar power. Isofotón was able to take advantage of the situation, supplying 15 percent of the German market. It grew to become the seventhlargest producer of solar cells in the world—but the global market has grown rapidly, and a handful of new companies have jumped in to fill the need. Isofotón's rank has now dropped slightly even as its business has expanded dramatically.

Spain has been one of the top world producers of solar cells for the past decade; the two main companies producing those cells are Isofotón and BP Solar, riencing rapid growth is Siliken, which is developing a silicon plant to ensure a steady supply of raw materials.

Traditionally, Spanish companies have exported about 80 percent of the cells they produced, but with renewed interest in PV within Spain, those numbers are changing. In only the last two years, nearly 100 megawatts of PV power have been added. Isofotón expects to sell about 60 percent of its panels within Spain, though the company still exports to Europe, North and South America, and Asia.

Jesús Alonso, Isofotón's director of research and development, says what distinguishes the company is the high quality of its cells. "You can find information in books about how to make solar cells," he says. "The main difficulty is the know-how—it's how to make sure that those 400 wafers you put in the furnace are actually good, quality solar cells. That's the key."

Like all solar-cell producers, Isofotón has been limited lately by the dearth of highly purified silicon necessary both for microelectronics and the solar industry. In response, it has begun setting up silicon refining operations in Cadiz, which should begin production in 2008

Working with Antonio Luque's IES, Isofotón has focused its research on developing concentrating PV cells. Downstairs in the factory, in a small room on the main factory floor, a machine whirs as thin sheets of one-millimeter solar cells pass through a machine. The tiny cells will be attached to gold wires and then serve as the focus of the concentrating lenses.

large scale, so that fields of trackers can be set up to take advantage of the sun's angled rays.

The material used in concentrating photovoltaics is gallium arsenide, which is 50 times as expensive as silicon. But the cells demand just one-thousandth as much material, cutting costs.

When it comes to traditional PV panels, most companies focus on marketing to the developed world—where money is available for PV and the process is as simple as creating the product and selling it. But Isofotón has taken the lead in marketing solar power to the developing world. This year the company expects rural electrification to account for nearly a quarter of its market. Even the marketing works differently for this segment of the business: projects must be researched and appropriate financial models developed for each. Isofotón has rural electrification projects around South America, Morocco, Algeria, Indonesia, and South Africa.

Solar power in these poor, rural regions is not used simply for home electricity but also for applications such as water pumps and desalination. To maintain a lead in this area, Isofotón is not just relying on the decades of experience it has already built up; it's putting additional research into how best to couple solar power with those types of applications, since much of the existing equipment isn't appropriately built to work with an intermittent energy source.

"If we look to the really long term, I think that our main market will be rural electrification, because at the end these are the people who don't have electricity," says research director Alonso. "Most of



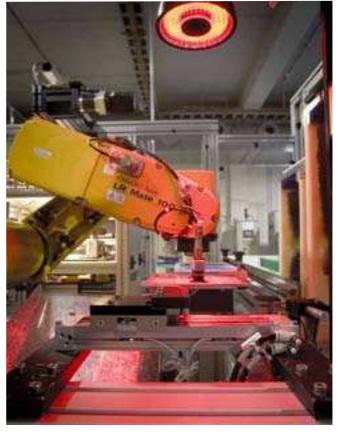


Top and bottom left: Isofotón's offices utilize solar power, with PV panels on the building's exterior and solar skylights. **Right**: Isofotón's robots create solar units.

the energy increase in the world will be in electricity, and most of that will be in developing countries."

Acciona Solar, the solar-energy arm of Acciona Energía, has seen phenomenal growth rates, as have the other major companies involved in this field. The company's income exploded from about half a million euros to more than 96 million euros in only eight years.

Last December, the company connected the Monte Alto Solar Field to the grid; it's the largest installation of its kind



PHOTOS COURTESY OF ISOFOTÓN

in Spain, and one of the largest in the world. It consists of a field of standard PV panels on trackers (which leads to 30 percent greater efficiency), spread out over a long-disused agricultural field in the southern part of the state of Navarra, about an hour south of Pamplona.

This is the latest of these fields, known as "huertas," or gardens, in Spanish. The 9.5-megawatt facility at Milagro actually has more than 750 owners—investors from across Spain, each of whom owns one or two of the panels and trackers and receives payments from the electric utility.

Most Spaniards live in apartment buildings and share rooftops, so the options for investing in solar power are limited. "This way they can have the same opportunities as the rest of the world even if they don't have their own roof," says Miguel Arrarás, director of Acciona Solar. There are 10 such fields in Spain, of which Milagro is the largest so far, and three more about to enter the construction phase.

The region of Navarra, with local government support, has become a veritable center of renewable energy, with wind turbines arching over the rolling hills and solar fields stretching across open spaces. The region's PV capacity in watt peak per inhabitant is more than 20 times that of Spain as a whole, and nearly double that of Germany, the world solar leader. Seventy percent of Navarra's electricity is generated from wind and solar alone.

Because of this, Navarra has become a perfect site to evaluate the entire system. "We're testing 30 different kinds of panels," says Arrarás. "We also have data on the effects of shadows, fog, everything. We have an agreement with two universities just to analyze this data." He continues, "This is also the perfect place to evaluate what the effect is on the entire grid when, say, there are clouds, because of the high concentration of solar power here."

The company's operations are housed in a zero-emissions building on the out-skirts of Pamplona. The building's design incorporates techniques, such as natural light and carefully placed shading, that reduce energy needs by 52 percent com-

pared with those of a typical building. The remaining energy is produced with PV cells, solar water heating, and a small amount of biodiesel. The investments will pay off in 10 years, according to Arrarás. Thanks to the company's experience, Acciona Solar is also researching ways to improve and promote these high-performance buildings.

Acciona is poised to begin construction on a PV solar field in Portugal that will produce nearly 50 megawatts—five times as much as Milagro.

Looking ahead

The Spanish government continues to promote investment in and expansion of both photovoltaic and solar thermal power, with a goal of 400 megawatts of installed power for PV and 500 megawatts for solar thermal by 2010. This still represents only a fraction of the country's total power use and total renewable production.

The government, however, is committed to advancing the sector. The new building code of 2006 requires increased energy efficiency and includes an obligation to meet a significant part of the hotwater demand with passive solar heating. And the Renewable Energy Plan sets a lofty goal of 5 million square feet of solar collectors by 2010. A royal decree approved in May 2007 improves the feedin tariffs for both solar thermal and PV facilities. Some experts believe that these developments could lead Spain to become the world's second-largest PV market in 2007. Spanish companies and research institutions plan to remain at the forefront of the growing global field.

Says Javier Anta, president of the Spanish Photovoltaic Industry Association, "The solar industry will be a major part of the government's goal of 20 percent renewable energy by 2020. Despite the fact that solar is only a small percentage of renewable power, it's grown more than 100 percent a year in the past few years." In fact, the sector grew 200 percent in 2006. He continues, "We're facing a grand challenge: consolidating that which we've achieved so far, setting the framework for future development, and creating a sector that makes our country proud."

Resources

ICEX (Spanish Institute for Foreign Trade) www.us.spainbusiness.com

Acciona Energía

www.acciona-energia.com

Atersa

www.atersa.com

Institute for Solar Energy www.ies.upm.es

Isofotón

www.isofoton.es

SENER

www.sener.es

Siliken

www.siliken.com

Solar Platform of Almería

www.psa.es

Solúcar

www.solucar.es

Spanish Photovoltaic Industry Association

www.asif.org

To find out more about New Technologies in Spain, visit:

www.technologyreview.com/ spain/solar

For more information visit:

www.us.spainbusiness.com

Contact:

Mr. Enrique Alejo Trade Commission of Spain in Chicago 500 N. Michigan Ave., Suite 1500 Chicago, IL 60611, USA T: 312 644 1154 F: 312 527 5531 chicago@mcx.es



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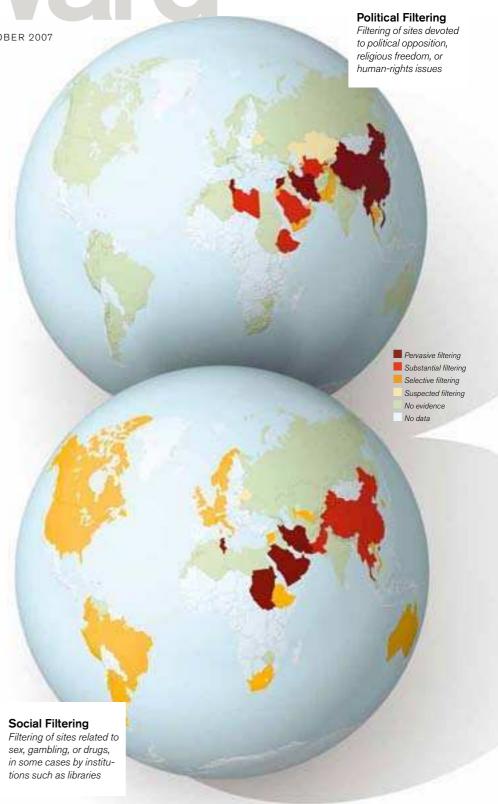
INTERNET

Mapping Censorship

Internet filtering around the world has grown in scale, scope, and sophistication in recent years. These maps, based on a study by an academic consortium, describe the extent to which nations block or restrict online content ranging from political dissent to porn. "Over the course of five years, we've gone from just a few places doing state-based technical filtering ... to more than two dozen," says John Palfrey, executive director of the Berkman Center for Internet and Society at Harvard Law School.

The OpenNet Initiative—a collaboration among researchers at Cambridge, Oxford, Harvard, and the University of Toronto—carried out its study in 2006 and early 2007 using technical tools that test filtering. The group also used reports from local researchers in some countries. Of 41 nations tested, 25 were found to block or filter content to various extents.

China, Iran, and Saudi Arabia remain top blockers, stamping out porn, political, human-rights, and religious sites. Other countries target specific categories: for example, Libya filters political content. In western nations, the story is more nuanced: U.S. libraries block some sites, and private parties remove copyrighted material to avoid lawsuits; in Germany, Nazi sites are banned. See opennet.net for details. Clark Boyd



Forward



WIRELESS

Shopping Search

A new mobile-phone service claims to be the first to offer location-aware search for products, not just for stores. The service, called Slifter, uses GPS-enabled cell phones; alternatively, a user can enter his or her zip code. The phone then displays lists of products that can be sorted by proximity or price.

During a recent test of the service, a search for a Nikon D40 accurately showed many nearby stores selling the camera. The Slifter search noted how far each store was from the phone and showed that all stores were selling the Nikon D40 for \$599.

Slifter could make price comparisons easier, but its databases are far from complete and the search results not always useful. A search for "ice cream" returned information on a toy store selling a product that had "ice cream" in its name. And the first hit in a search for "iPod Nano," performed in Cambridge, MA, was for an iPod accessory 26 miles away.

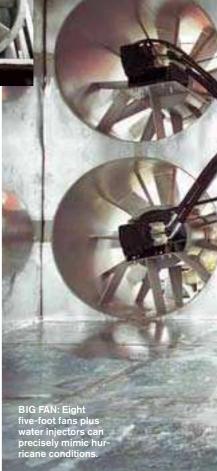
Jeremy Kreitler, director of product management for Yahoo Maps, says the big search players aren't yet attempting Slifter-like services because they don't have "great, comprehensive, clean data" on inventories. Outside the realm of consumer electronics, data is often unavailable or of "questionable" quality, Kreitler says. —David Talbot



CIVIL ENGINEERING

Portable Hurricane

ngineers at the University of Florida, Gainesville, have built a machine that can crank out Hurricane Katrina-like conditions to test the sturdiness of structures and materials. The trailer-mounted apparatus sports eight five-foot fans powered by four 700-horsepower marine engines. A duct and rudders allow precise control of wind speed and direction; a water-injection system simulates wind-driven rain. Forrest Masters, a civil engineer at the university and a leader of the hurricane-simulator project, plans to use the machine to blast state-donated homes, building products, and trees. The data will be used to help Florida update its statewide building codes. Brittany Sauser



ENERGY

Plug-In Plans

Automakers are planning to develop hybrid vehicles that have large battery packs and can be plugged into electrical outlets for recharging, so they can run much farther on electricity alone than conventional hybrids can. But it will be years before factory-made models are available. Now, some institutions are funding their own plug-in R&D and even acquiring plug-in fleets by hiring companies to add larger batteries to existing hybrids and modify their electronics. —Kevin Bullis

Organization/location	Plug-in plan	Cost/number of vehicles
New York State Energy Research and Development Authority, Albany, NY	Convert state's existing hybrid fleet to plug-in, pending economic analysis	\$10 million/500
Google, Mountain View, CA	Fund plug-in R&D, gather data on plug-in performance, offer plug-ins to employees who carpool	\$11 million/100
California South Coast Air Quality Management District, Diamond Bar, CA	Develop small fleet; study expansion to 100,000 plug- ins by 2014	\$2.1 million/30

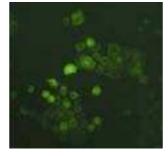


MEDICINE

Nano **Curry**

Encased curcumin could be used as drug

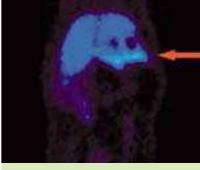
n recent years, laboratory and animal studies have suggested that curcumin the pigment that gives the Indian curry spice turmeric its bright-yellow huecould be useful for treating tumors, cystic fibrosis, and even Alzheimer's disease. But curcumin is insoluble and not readily absorbed



by the body, making it impractical as a drug.

Now researchers at the Johns Hopkins University School of Medicine and the University of Delhi, in India, have invented curcumin-carrying nanospheres that slip easily into the bloodstream. Anirban

Maitra, an associate professor of pathology and oncology at Johns Hopkins, and his collaborators in Delhi used polymers to make particles about 50 nanometers in diameter. The nanoparticles (*left*) have hydrophobic interiors that hold the curcumin and hydrophilic exteriors that make them more readily absorbed. Once the particles are in the blood, the curcumin leaks out as the polymers slowly degrade. Maitra and colleagues are now planning animal studies. Ganapati Mudur



Seeing Signs of Diabetes

cientists estimate that patients with type 1 or type 2 diabetes have already lost 50 to 90 percent of their insulinproducing cells by the time their conditions are diagnosed. A new molecular tracer could provide the first clear view of these cells in the pancreas, helping doctors detect and treat diabetes far earlier.

The tracer was developed by Hank Kung, a scientist at the University of Pennsylvania. It binds to a receptor inside the cells and is tagged with a radioactive label that can be detected using positron emission tomography (PET).

Preliminary tests show that PET scans using the tracer can distinguish between rats with healthy levels of insulinproducing cells in the pancreas (glowing areas in the image above) and rats whose insulinproducing cells have been chemically damaged.

"If we could see cell loss early, perhaps we could get patients started on therapy before there is irreversible damage," says Dan Skovronsky, founder and CEO of Avid Radiopharmaceuticals, the Philadelphia company that is developing the tracer.

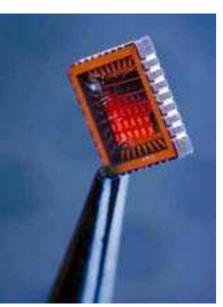
Avid aims to begin diabetes testing in humans this year. -Emily Singer

HARDWARE

Silicon-Based Spintronics

Today's computers work by moving and storing electronic charge. But manipulating another property of electrons, their quantum-mechanical "spin," would be faster and take far less energy. Researchers have been working on "spintronics" for years, and now electrical engineers at the University of Delaware and at Cambridge NanoTech in Cambridge, MA, have made the first prototype device that measures spin in silicon.

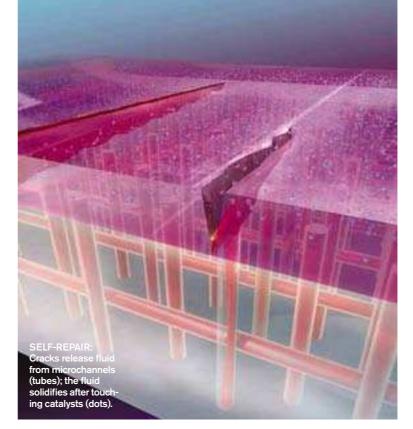
Electron spins come in two directions, up and



SPIN CHIP: An array of onemillimeter-square silicon spintronic devices sits in a chip carrier.

down, which could represent the 1 and 0 of binary computation if spin could be controlled and detected. In the prototype, energized electrons first hit a magnetic cobaltiron layer, which filters out electrons with down spin. The remaining up electrons pass through a 10-micrometer silicon layer and hit a detector consisting of a nickel-iron layer on top of a copper layer; all the layers sit on a silicon sub-

strate. "It's a very ingenious scheme to electrically generate and transport spins in silicon, [to] electrically detect the spins, and doing all of this on a chip," says David Awschalom, a physicist who studies semiconductor spintronics at the University of California, Santa Barbara. —Prachi Patel-Predd



MATERIALS

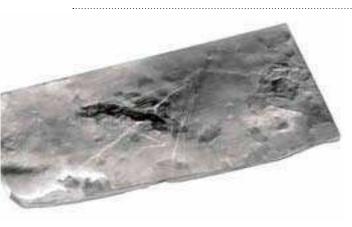
Self-Healing Plastic

A new polymer material that fixes its own cracks could be a step toward self-healing medical implants or self-repairing materials for use in airplanes and spacecraft. It consists of an epoxy polymer layer containing tiny catalyst particles, deposited on a substrate containing microchannels filled with a liquid.

When a crack in the polymer layer spreads to the microchannels, the liquid flows out and comes in contact with the catalyst, says Nancy Sottos, a professor of materials science and engineering at the University of Illinois at UrbanaChampaign and one of the researchers who led the work. Ten hours later, the liquid solidifies into a polymer.

Researchers have previously made self-healing plastics, but this is the first time anyone has made a material that can repair itself multiple times on its own. The material survived up to seven cracks before the catalyst stopped working.

"It's essentially like giving life to a plastic," says Chris Bielawski, a chemistry professor at the University of Texas at Austin. "This is an amazing proof of concept." Prachi Patel-Predd



ARCHAEOLOGY

Virtual Paleontology

This CT scan carries bad news: the patient has been dead for 220 million years. On the positive side, it reveals that the subject was long-necked, had grasping feet and fine bones, could glide, and probably lived in trees. Made with an industrial CT scanner at Penn State for researchers at the Virginia Museum of Natural History, this image of a previously unknown reptile is the first to depict a Triassic fossil whose encasing rock has not been cracked away. The technique, which requires the precise focusing of the scanner's x-rays, could become a standard tool as paleontologists dig deeper for new finds. —Erica Naone



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SOFTWARE

Invisible Ink from Xerox

Researchers at Xerox have come up with a way to add fluorescent words and images to documents like checks, coupons, and transcripts using standard printers. The technique makes it possible to create everyday documents that have telltale marks visible only under ultraviolet light.

Bright white paper is often fluorescent to begin with; the new process exploits that fact by printing the same shades of color in different ways, leaving more or less paper exposed. For example, in standard color printing, which uses cyan, magenta, yellow, and black inks, a gray tone can be produced with lots of the first three and very little black. But it can also be produced with more black



and a little color plus the white of the bare paper, which will fluoresce under ultraviolet light. The same technique can yield a wide range of shades, each produced by multiple combinations of the four ink colors.

The technology boils down to "finding different combinations of

the four colors that present the same visual color but provide very different page coverage," says Reiner Eschbach, research fellow at the Xerox Research Center Webster. The necessary software will be incorporated into high-end commercial printers. David Talbot

WHAT DO YOU SEE?



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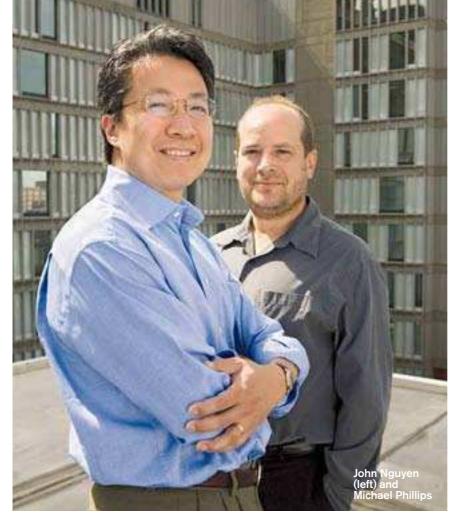
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STARTUP

Talk to the Phone

Vlingo's voice-recognition interface unlocks the mobile Web

obile phones can do lots of things: search the Web, download music, send e-mail. But the vast majority of the 235 million Americans who own them never use them for more than calls and short text messages. One reason is that other features often require users to enter sentences or long search terms, a tedious task.

Speech-recognition interfaces could make such features easier to use. Vlingo, a startup in Cambridge, MA, is coming to market with a simple user interface that provides speech recognition across mobile-phone applications. "We are not developing the core speech-recognition engine," says cofounder Michael Phillips, a

former MIT research scientist and founder of SpeechWorks, which developed call-center speech interfaces for clients including Amtrak. "We don't need to do that again." Instead, Vlingo takes speech, turns it into text, and provides a simple way to correct errors using the phone's navigation keys, helping the system "learn." The user's spoken words travel over a mobile Internet connection for analysis on Vlingo's server, sparing the phone the heavy computational work; the transcription appears less than two seconds later.

As a test, I asked the phone for "Schumann Piano Concerto." Vlingo came back quickly with "Sean Piano Concerto." When I hovered the cur**Company:** Vlingo, Cambridge, MA **Funding:** \$6.5 million from Charles River Ventures and Sigma Partners

Founders: Michael Phillips, SpeechWorks founder and former MIT research scientist; John Nguyen, former SpeechWorks computer scientist

CEO: David Grannan, former manager of mobile e-mail at Nokia

sor over the word "Sean," the system offered alternatives like "shine" and "sign." If one of them had been right, I could have clicked to insert it as a replacement. But since the right word didn't appear, I typed it in manually.

My correction upped the chances of better results in the future. I had taught the system that the next time I use a word that sounds like Schumann, "Schumann" should be one of my optional transcriptions. I also taught it that other people conducting music searches might use the word "Schumann"—so it might start popping up for them, too.

"Small platforms need speech, and search is a powerful way to find information," says James Glass, head of the spoken-language systems group at MIT's Computer Science and Artificial Intelligence Laboratory. "The combination of the two is very powerful," he says, adding that Vlingo is working at that frontier.

Vlingo wants mobile-phone carriers to bundle its interface with other offerings. "Carriers may be happy to give it away, because they will generate revenue as people actually use navigation systems or surf the Web," says CEO David Grannan.

Mazin Gilbert, executive director of natural-language processing at AT&T Labs in Florham Park, NJ, says others, including AT&T, are also developing speech interfaces for mobile phones; he thinks one problem will be "providing the right user experience in a cost-effective, scalable way." Vlingo thinks a simple, adaptable interface is one way to make growth easy. **David Talbot**



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WEDNESDAY, SEPTEMBER 26

Keynote Panel: Game Changers

Suranga Chandratillake, Cofounder and CTO, **Blinkx; Tariq Krim**, Founder, **Netvibes**; **Kevin Rose**, Founder and Chief Architect, **Digg.com**Don't miss this fresh, innovative panel as these innovators unveil what's next for their companies and reveal the impact it could have on yours.

Keynote Panel: What's the Big Idea?

Prith Banerjee, SVP, Research, and Director of HP Labs, **Hewlett-Packard**; **Andrew A. Chien**, VP of Research, **Intel**; **Guido Jouret**, CTO, Emerging Markets Technology Group, **Cisco Systems**

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Keynote

Charles Simonyi, Cofounder, **Intentional Software Corporation**; **Bob Metcalfe**, General Partner, **Polaris Venture Partners**

Metcalfe and the developer of Microsoft Office discuss the future of software.

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THURSDAY, SEPTEMBER 27

Opening Keynote

Sky Dayton, CEO, Helio

Helio's mobile strategy and creative flair are unmatched in today's mobile market. Hear about Dayton's vision for the future of mobile.

Keynote

Gilberto Gil, Minister of Culture, Brazil

How can technology influence and strengthen culture? Minister Gil addresses topics like Brazil's commitment to "free culture," open-source software, and the \$100 laptop.

Keynote Panel: Creating Media

Guillaume Cohen, CEO, Veodia; Di-Ann Eisnor, CEO, Platial; Carlos Garcia, CEO, Scrapblog; Dan Gillmor, Founder, Center for Citizen Media

What's next for personal publishing? Leaders of top content-creation companies discuss their technologies with live demonstrations.

Fireside Chat

Ann Winblad, Partner, Hummer Winblad Venture Partners

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Hack

Apple's iPhone

An inside look at a sensation By Daniel Turner

pple's latest offering proves that revolutionary tech products don't have to be *that* revolutionary. Upon the iPhone's release, enthusiasts around the world rushed to tear it apart, eager to see something new. Instead, they found that Apple had relied mostly on tried-and-true components—with one big exception: a truly stunning multitouch screen that allows users to manipulate data and images in entirely unprecedented ways.

(B) Communications Center

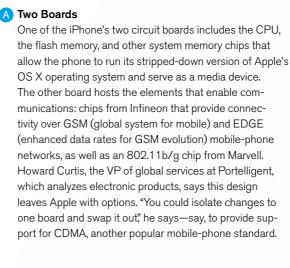
The chips that make the iPhone a phone "seem to be pretty standard," says Kyle Wiens of iFixit, an online Apple parts retailer. Portelligent's Howard Curtis agrees: "They're plain vanilla." A standard Infineon Technologies processor supplies the EDGE wireless-data capabilities and supports the camera and the movie playback system. There's also a transceiver for quad-band GSM connectivity. Marvell's chip is accompanied by a Cambridge Silicon Radio chip that offers Bluetooth 2.0. Critics scorn the iPhone for not working with AT&T's 3G network, but Apple has said that incorporating 3G hardware would add heat and reduce battery life. Wiens says the real issue is that 3G "is practically nonexistent outside large cities." Still, he adds, Apple will need to address this issue if it wants to sell the iPhone in Europe.





Accelerometers

Like Nintendo's Wii game console (see Hack, July/August 2007), the iPhone uses miniaturized accelerometers that measure its movement. These sensors detect whether the user is holding the iPhone in its "portrait" or "landscape" orientation; the operating system rotates the display accordingly.











Multitouch Display

Apple has had problems with the plastic screens on its iPods, which tend to show scratches, but the iPhone's screen is made of optical-quality glass. That's all the more critical because the screen is the interface. Instead of buttons or a keyboard, the iPhone uses a combination of new software and a unique multitouch screen manufactured by the German company Balda. Users tap "soft" buttons directly on the screen and zoom in or out of images or Web pages with two-fingered gestures (zoom out is a pinch, zoom in is a spread). This new control scheme abandons the WiMP (window, icon, menu, pointer) system that has dominated graphical interfaces on computers for decades.

CPU

The phone's brain is a custom-for-Apple CPU built by Samsung and based on a 32-bit, 620-megahertz core from ARM, which makes dedicated systems for use in cars, handheld games, smart cards, and other applications where power is at a premium. Howard Curtis says that working with ARM, a company prominent in the "embedded" market, could be significant for Apple. "OS X is now in the embedded space," he says, even as Microsoft keeps trying to build a desirable version of Windows for the same market.

Battery

Though the iPhone's lithium-ion battery is nothing new technically—"it's just like the battery in an iPod, but big, very big," says Wiens-it has gotten a lot of attention. That's because unlike the batteries in other cell phones, the iPhone's is soldered on and not (easily) replaceable by the user. (Apple will change a dead battery for \$79 plus shipping.) At least one consumer has filed suit against Apple for its battery policy. Apple executives say that even after 400 complete depletion-and-recharge cycles, the battery will retain 80 percent of its charge capacity, which should be good for well over six hours of talk time.

Alieu Conteh

Building a mobile digital network in Congo

lieu Conteh, the chairman of Vodacom Congo, created a mobile digital communications network in a country where none had existed. In 1999, when he launched what was then Congolese Wireless Network (CWN) with just 4,000 subscribers, his nation must have seemed hopelessly ill suited for any investment in technology.

The Democratic Republic of Congo is about the size of Western Europe and has an estimated population of 65 million. But it is one of the least developed nations in the world, with less than 2,000 miles of paved roads. In 1999, fewer than 15,000 houses had land-based telephones, and no more than 10,000 people had analog mobile handsets.

In building his company, Conteh faced challenges unknown to communications executives from the rich world. Once, after equipment providers declined to send engineers to Congo during a particularly dangerous time in the country's unending civil war, Conteh encouraged a group of citizens in Kinshasa to collect scrap metal and weld it into a cell-phone tower.

In 2001, Conteh and Vodacom, South Africa's largest mobile-service provider, formed a joint venture in which Vodacom would hold 51 percent of the new company. By the middle of 2006, Vodacom Congo had more than 1.5 million subscribers, according to Vodacom's annual report. Today, according to Conteh, the company he founded has more than two million subscribers. He claims that a recent offer for his shares valued Vodacom Congo at more than \$1.5 billion.

Technology Review's editor in chief met Alieu Conteh by chance at a technology conference in Tanzania. In person, Conteh, who is 55, appears optimistic, cheerful, vital. He is also richly amused by his own story. While grateful for his extraordinary good fortune and proud of his contribution to his country, he also relishes the human comedy of the founding of Vodacom Congo.

TR: Before this, had you ever worked in communications?

Conteh: I exported coffee beans. But during the civil war in Congo, I lost everything in the countryside to the rebels. When Father [Laurent Désiré] Kabila took power [in May 1997], he made a famous speech in Kinshasa. He spoke about zero tolerance for banditry and corruption, and about how Congo needed very basic things: law and order, education, roads, and telecommunications. I was very impressed with that speech.

You were inspired?

I was. I started to think about telecommunications. I knew the reconstruction of the infrastructure of Congo was going to need billions and billions of dollars. Maybe the whole world would have to help. But I started thinking: I was one of the few people in Congo who owned a mobile handset. The people who had handsets were mainly government ministers and their staffs, the military, expats, and a few businessmen like myself. My phone cost me \$1,200 and I paid \$15 a minute for every call. I saw it as an opportunity. What did you do?

Two or three weeks after Father Kabila's speech, a friend introduced me to the minister [of post and telecommunications, Kinkela Vinkasi]. I asked the minister if I could submit a proposal for a mobile license.

He asked, "What type of license?" I said, "GSM." [The Global System for Mobile communications—the most popular standard for mobile phones.] The minister was nice but firm: he said I had to provide proper documentation. And as he walked me to the door, he said, "Mr. Conteh, you understand that to build a GSM network, it's a lot of money!" I said, "If the government will grant a license, I will build a network."

What happened next?

Well, I knew zero about telecommunications. I asked my secretary, "Mrs. Baba, do you know anybody in telecom?" She said she did. This man, Gilbert Nkuli, who became our first employee, went to the minister of communications and filled out the forms. I called another friend and asked him, "Do you know any telecom vendors?" He said he knew a single vendor, Nortel. We phoned Nortel in Paris. A Nortel executive said, "Send me a letter of invitation; otherwise I can't get a visa." I did. A week later, he was there.

He was keen.

It seemed so. Well, the three of us, we all went to see the minister. We explain how we're going to provide cell coverage for Congo's main cities. Four months later, the minister calls me into his office and tells me that the government has approved the license, but before they can issue it, I must pay \$100,000.

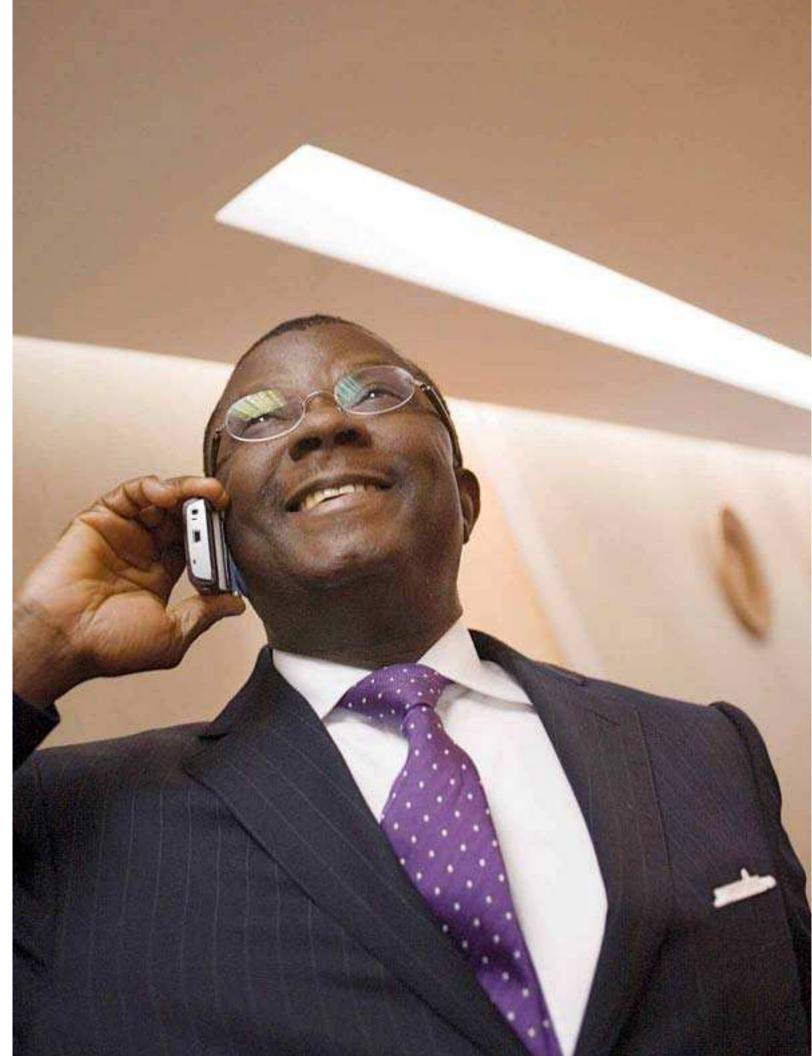
For an exclusive license?

To tell you the truth, I didn't know. I'd never seen a telecommunications license before. But the government wanted \$100,000 in American dollars to be paid to the central bank. I found the money. Three months later, the minister calls me again. Now he says, "Conteh, you have to pay another \$100,000." So I paid \$200,000, but I still did not have the license.

It was a shakedown.

Wait! It gets funnier. In January of 1998, all the big government ministers

32





went to a conference in Uganda on pan-African concerns. When they got back, the minister of communications phoned me and said, "The Ugandan government sold their GSM license for \$8 million, and Uganda is a small country. So our license is \$8 million"! I kept my cool. I said, "Okay. Give me a few days." A week later I went to the minister and said, "Your honorable minister ... \$8 million for Congo? In the future, maybe. Today, no." He asked, "Why?" I said, "The war is why. Everything is broken. Everybody is leaving the country." Finally, he listens to me. He asks, "Well, Conteh, how much can you pay? What do you think the license is really worth?" I have to be fair. I say \$2 million. He called me that evening at 10 o'clock to tell me I'd got a 20-year license to operate a GSM network in Congo. And then?

Well, of course, that was just the beginning. We asked Nortel to do a study about the costs of creating the network. We talked to GTE. We hoped one of them would be our partner and invest in this idea of a Congolese GSM network. But eventually I had to be honest with myself; I had to accept that no vendor was going to put money in Congo. I went home; I

asked my wife. The only savings I had was \$1.5 million. She said I should follow my heart. That was so dear, so dear to me and painful. In the end, I went with Nortel. I went to Paris. I carried my checkbook with me. How did you feel writing a personal check for so large a sum?

After I wrote the check, Nortel threw a party with champagne. All the Nortel executives in France were there. They wanted to know: who is the man behind this thing? Before the speeches, the president of Nortel tried to give me a glass of champagne. I said I needed water. I told him, "The day my network is done I'll drink something, and not before."

After you'd spent your savings, you still needed capital for staff, vehicles, offices, and so on. What did you do?

I sold everything: my coffee trucks, my personal car, everything. We never had enough money in

I look at the minister,

very first digital tele-

telephone will never

phone in Congo! The

again be a luxury in this

phone to the minister

because I was so ner-

vous, sweating blood.

country." Then I gave the

and I say, "I am pleased

to announce today the

the beginning. At one point, I had to tell everyone who worked for us that I couldn't pay their salaries, but if we stuck together we would be all right in the future. You know, most stayed! And today, they've all bought houses.

Tell me about how you finally launched

the Congolese Wireless Network.

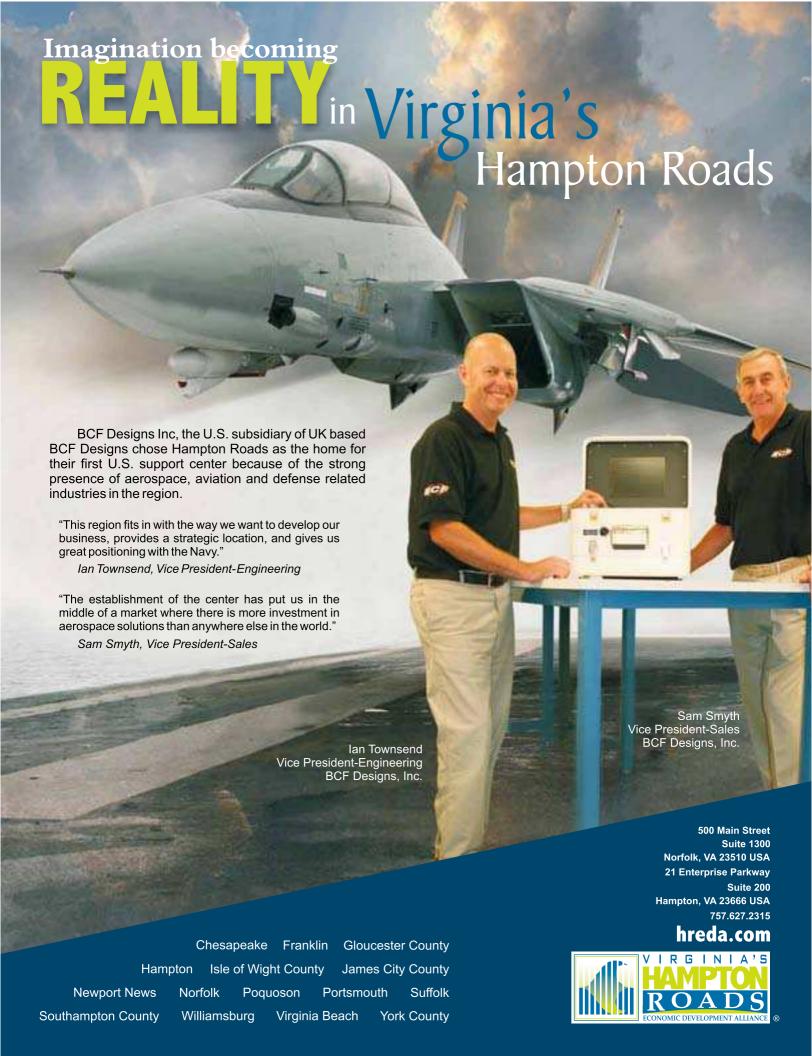
The day before, tests had been going fine. I go to see the switch. I'd put it in a modern one-bedroom apartment in Kinshasa, because it would be safe there. But when I walk in the room, the engineers are very nervous. The switch isn't working! CWN is due to be announced the next morning, at 11:00 A.M. [on February 20, 1999]. The engineers work all night; I had a Congolese grilled-meat dinner brought to them. But Saturday morning it's

still not working. The whole government has come to the ceremony at the Hotel Memling in Kinshasa. Every embassy is there. But I'm still sitting in my office. I have a GSM phone in one hand and an analog phone in the other, and I'm talking to the engineers on the analog. It's 20 minutes to 11:00 a.m. I joined the minister and his delegation. Now he's worried, too. He's asking, "Should we postpone?" I say, "No, no. It's going to work fine."

So, at five minutes to 11, we go into the hall. We sit down on a sort of stage. The state minister representing the president of the republic is there. The Nortel representative is there. Journalists are taking photographs. The minister is hitting me on the shoulder and saying, "Conteh, can we stop this?" I think, if I panic, it is finished. And if I don't operate the network today, it's finished, too. Just at that moment, my

GSM phone rings. I say, "Hello?"
The Nortel engineer, a French guy, says, "Mr.
Conteh?" I say,
"Yes ..." He says,
"This is Sébastien.
It's working!" I say, "Sébastien, for God's sake, don't turn the phone off, stay on the line."
And I look at the

minister, and I say, "I am pleased to announce today the very first digital telephone in Congo! The telephone will never again be a luxury in this country." Then the crowd goes *pah pah pah pah*. Then I gave the phone to the minister because I was so nervous, sweating blood. The minister says, "Sébastien, Sébastien? The whole Congolese nation is listening to you! Thank you so very much!" And then at last the minister gave the phone to Kabila's representative, who spoke to Sébastien. JASON PONTIN



THE INTERNET

Protecting Security and Privacy

Tadayoshi Kohno considers the risks of ubiquitous computational devices.

We are at the cusp of a technological revolution that will make computational devices ubiquitous in our environment—from digital sensors for home-based assisted living to next-generation wireless implantable medical devices for heart pacing and defibrillation. But the wonderful new opportunities these devices present come with potentially serious threats to our data, privacy, prop-

erty, and even personal safety. For example, while the MySpace generation might flock to future phone-based social-networking systems—systems that could instantly reveal whether the person next to you at the bar is a "friend of a friend" who shares your

passion for classic movies and country line dancing—those same systems might be exploitable by sexual predators and other miscreants.

Helping society realize the benefits of these new technologies without simultaneously exposing users to serious risks is the charter of the computer security research community.

Computer security researchers study existing and proposed electronic systems in order to determine and learn from their weaknesses. In my own work with colleagues at Johns Hopkins and Rice University, we discovered that it's possible to compromise the security of electronic voting machines and change election results. In another example, scientists at Microsoft Research have evaluated the extent to which malicious software on cell phones could disrupt regional cellular communications.

Once we've identified significant security deficiencies, we develop improved security mechanisms. Classically, such research has centered on systems that *can* be used securely. But there is a wide gap between systems that can be used securely and systems that *will* be used securely. For example, recent results from Harvard University and the University of California, Berkeley, suggest that many users ignore anti-phishing defenses in Web browsers. To fully understand and improve the usability of security mechanisms, we must study users in realistic settings. At the University of Washington, we developed a building-wide network of sensors—

> the RFID Ecosystem—that we are using to explore more intuitive and natural methods for controlling digital privacy in future computing environments.

Another emerging theme in security research is the attempt to hold computer users accountable—to find digi-

tal analogues for surveillance cameras and forensic identifiers like fingerprints and DNA. Together with researchers at the University of California, San Diego, my colleagues at the University of Washington and I are developing one such accountability mechanism. Our design preserves a user's privacy in the common case: while they're always present, our forensic trails can be "opened" only under very special circumstances—for example, when a court order has been issued.

The next time you're enjoying the benefits of your latest digital gadget, whether it's a wireless gaming helmet with built-in brain-activity sensors or a new RFID credit card, you might think about the mischief that could be accomplished by someone who circumvents the device's security. The helmet could let you

directly control your computer game with your mind, but could it also reveal your private thoughts to malicious software on the gaming system, or to anyone within wireless range? These are the kinds of issues that drive the security research community toward creating a more secure and private digital world.

Tadayoshi Kohno, an assistant professor in the Department of Computer Science and Engineering at the University of Washington, is a member of the 2007 TR35 (p. 58).

NANOTECHNOLOGY

The Future of Manufacturing

Production of complex systems will soon take advantage of self-assembly, says **Babak A. Parviz**.

A typical microprocessor integrates a large number (greater than a hundred million) of small (less than 100 nanometers) electronic parts, but the miniaturized systems of the future will also need to incorporate photonic, mechanical, chemical, and even biological devices. The semiconductor industry has had impressive success in producing integrated electronics, but it has been decidedly less successful at mass-manufacturing multifunctional microsystems, partly because the processes used to make different components are incompatible. A major question for engineers is what manufacturing process can mass-produce useful multifunctional, miniature systems. The conventional approach to making engineered products is unlikely to yield a satisfying answer.

The most complex functional systems are found in the biological world. Nature is full of machines with trillions of nanoscale components all working in harmony. The complexity and sophistication of biological machines—in terms of the number of parts, the variety of materials used, and the diversity of functions

performed—is far beyond what any microfabrication or nanofabrication can achieve.

These advanced biological machines are mass-produced in a way that is fundamentally different from the

way we produce products such as microprocessors, automobiles, or airplanes today. In nature, components "self-assemble" to yield complex functional systems. Inspired in part by this observation, a number of research groups are working to enlist self-assembly as a method for producing functional products across size scales. The hope is to create a new paradigm in mass manufacturing in which self-assembly replaces assembly of parts one by one. We believe that, in principle, it is possible to "grow" an integrated circuit, a biomedical sensor, or a display.

To get a system to self-assemble from the bottom up, you have to address a few key issues: how the parts are made, how they are induced to recognize and bind to each other in the correct fashion, and how the assembly process can be controlled and streamlined. Chemical synthesis can readily produce a large number of nanoscale "parts" such as quantum dots or molecules that are designed to perform specific functions. And researchers can take advantage of specific covalent bonds or supramolecular bonds such as DNA hybridization or protein-inorganic surface interactions to program the self-assembly process.

Our group has investigated these methods as a way to produce hybrid organic-inorganic transistors and photonic waveguides. Solid-state microfabrication is another technique for producing parts for self-assembly. The parts are fabricated

separately, released, and then induced to self-assemble. Our group has used this approach to construct high-performance silicon circuits on plastic.

This revolutionary manufacturing method offers many opportunities. Growing machines may not be as farfetched as it once seemed.

Babak A. Parviz is an assistant professor of electrical engineering at the University of Washington. He is also a member of this year's TR35 (p. 70).

BIOTECHNOLOGY

Cells by Design

J. Christopher Anderson explains the importance and the challenges of synthetic biology.

Living cells are amazing things.

They created the oxygen we breathe and the fossil fuels that power our world. They provided the organic compounds that form the basis of many drugs and materials. They feed us, live in our bodies, and protect us from other cells and viruses. They can self-organize. They can learn.

It's clear, then, that the potential range of what biological systems *could* do is enormous. Among the areas that could most obviously benefit from them are health care, chemical and materials production, environmental remediation, and energy. However, most of the systems that would be useful in these areas are unlikely to occur naturally. We probably won't stumble upon a cell capable of serving as an artificial blood substitute, for example, or one that harnesses sunlight as transportation fuel. These systems must be engineered.

Synthetic biology seeks to build non-natural systems by adding DNA sequences—effectively, little genetic "programs"—to well-studied cells such as *E. coli* and yeast. This is, at heart, an engineering problem, one that

requires both new "software" (new sequences of DNA) and new hardware (the DNA itself—and the methods for putting it into cells). Synthetic biology has thus far dealt principally with the software. But making the DNA that can be put into cells is difficult and expensive; it has been the fundamental impediment to progress.

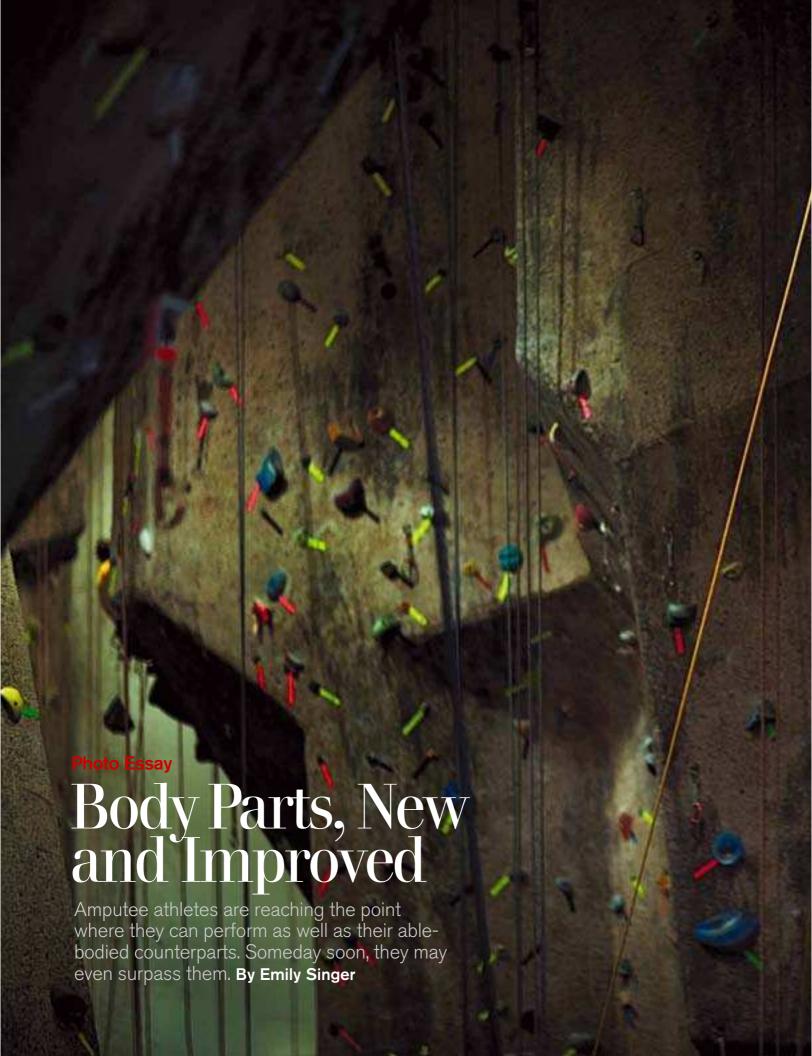
Today, long sequences of DNA can be synthesized chemically by commercial vendors at a cost of \$1 per base (the DNA "letters" A, T, C, and G). Considering that the sequences we design today are on the order of 10,000 bases, and we want to redesign entire four-megabase genomes, the costs quickly become astronomical. We hope the price will drop, but an alternative lies in the automated assembly of standard biological parts. Here, we don't synthesize each DNA program with base-level precision. We instead begin with a library of "basic part" DNA sequences. A robot joins these sequences into complete genetic programs using a standard assembly reaction. It is analogous to building electronic devices from a box of transistors, capacitors, and resistors rather than building the whole system at

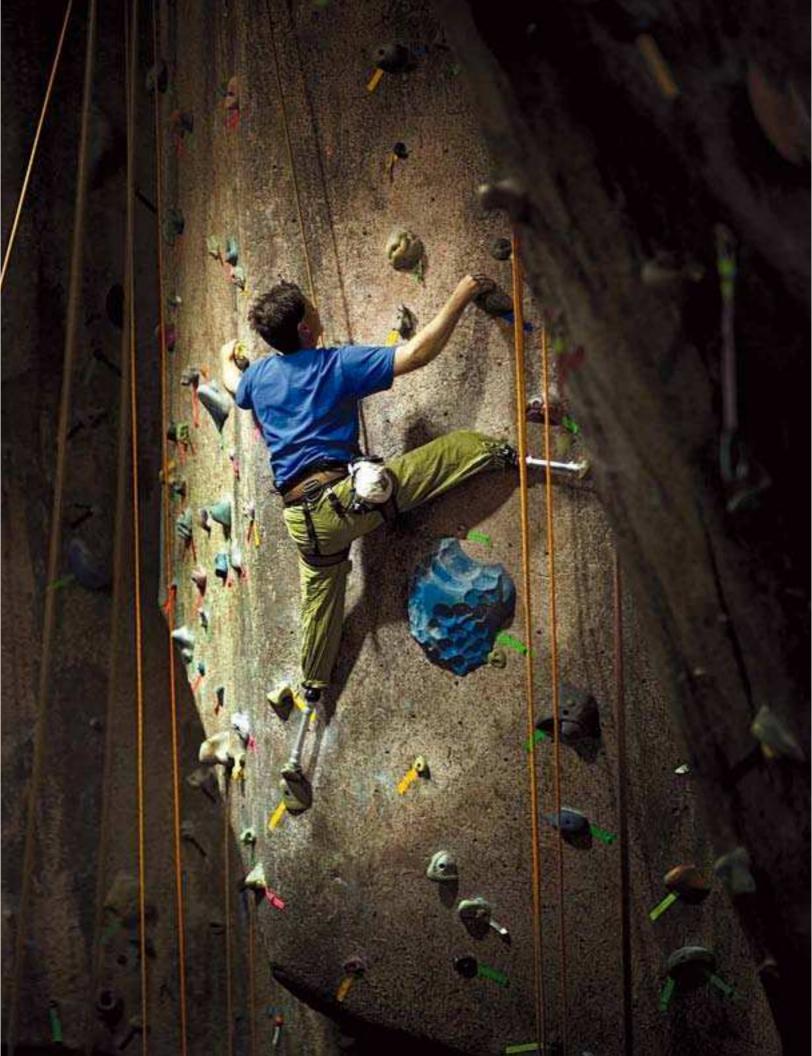
once by lithographic methods. The key is making the technique robust, low cost, and highly automated.

Synthetic biology will really take

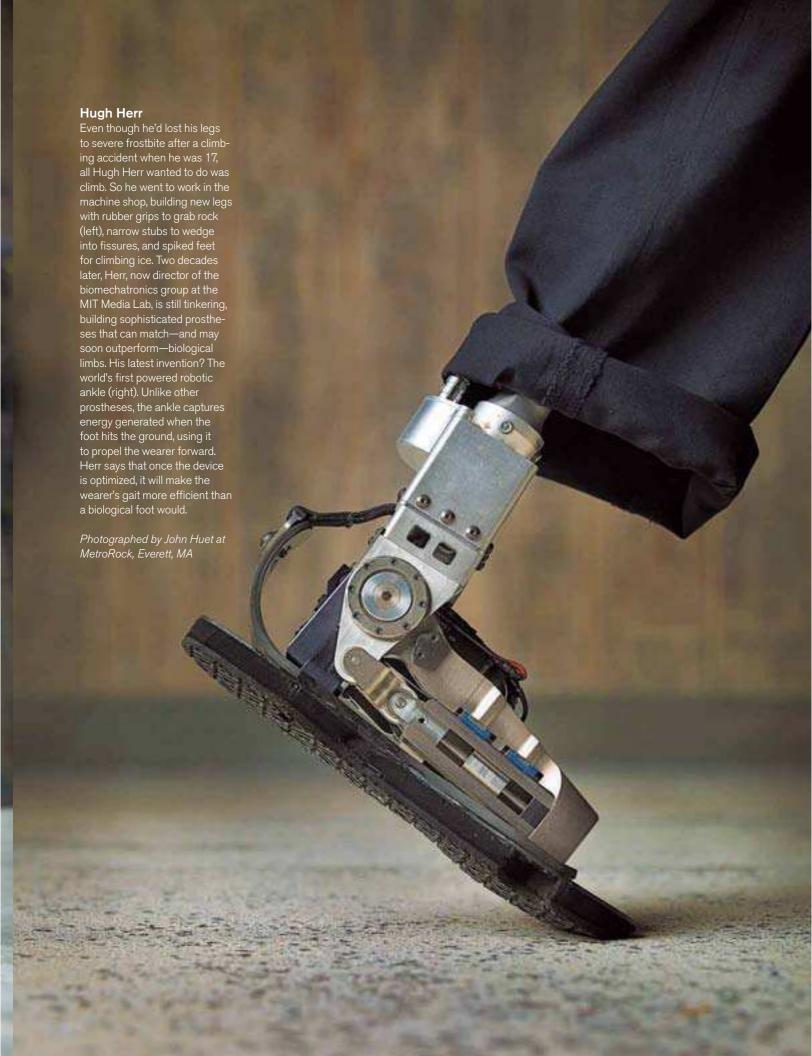
off once it has transformed itself into an information-driven discipline. The key to that transformation is automated synthesis. The potential is clear—we have no shortage of naturally evolved examples that tell us where the technology *can* go. We just have to figure out how to take it there.

J. Christopher Anderson, a member of the 2007 TR35 (p. 60), is a postdoctoral fellow in the Department of Bioengineering at the University of California, Berkeley.



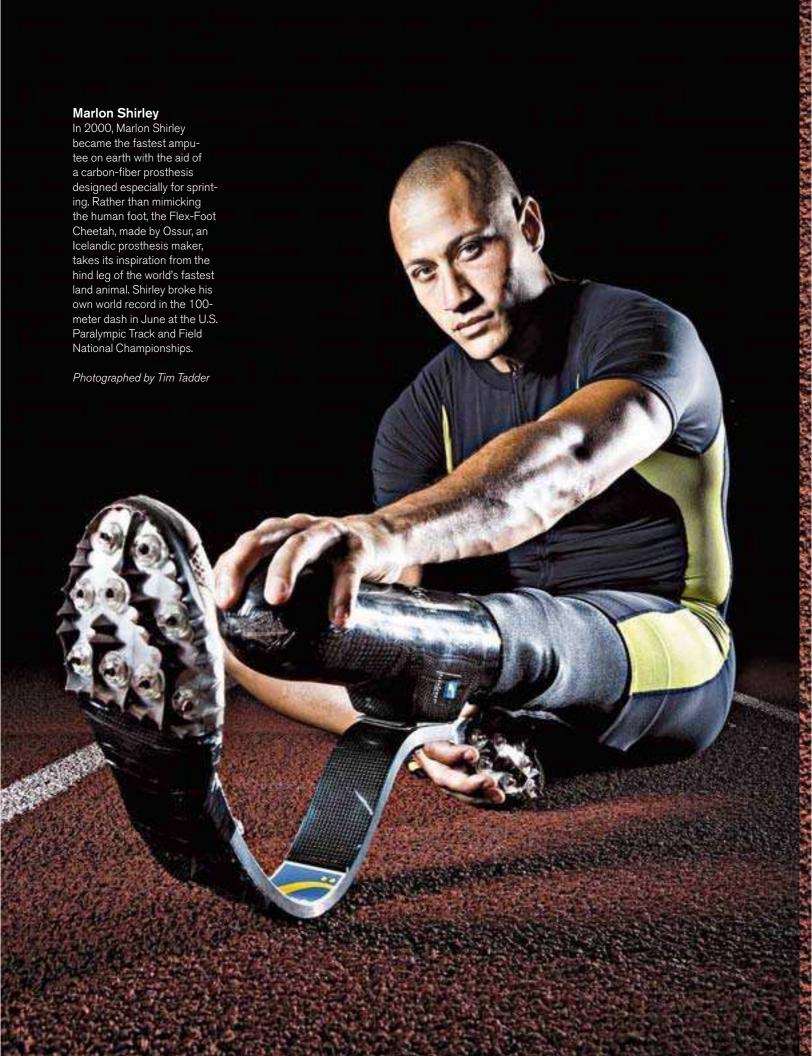


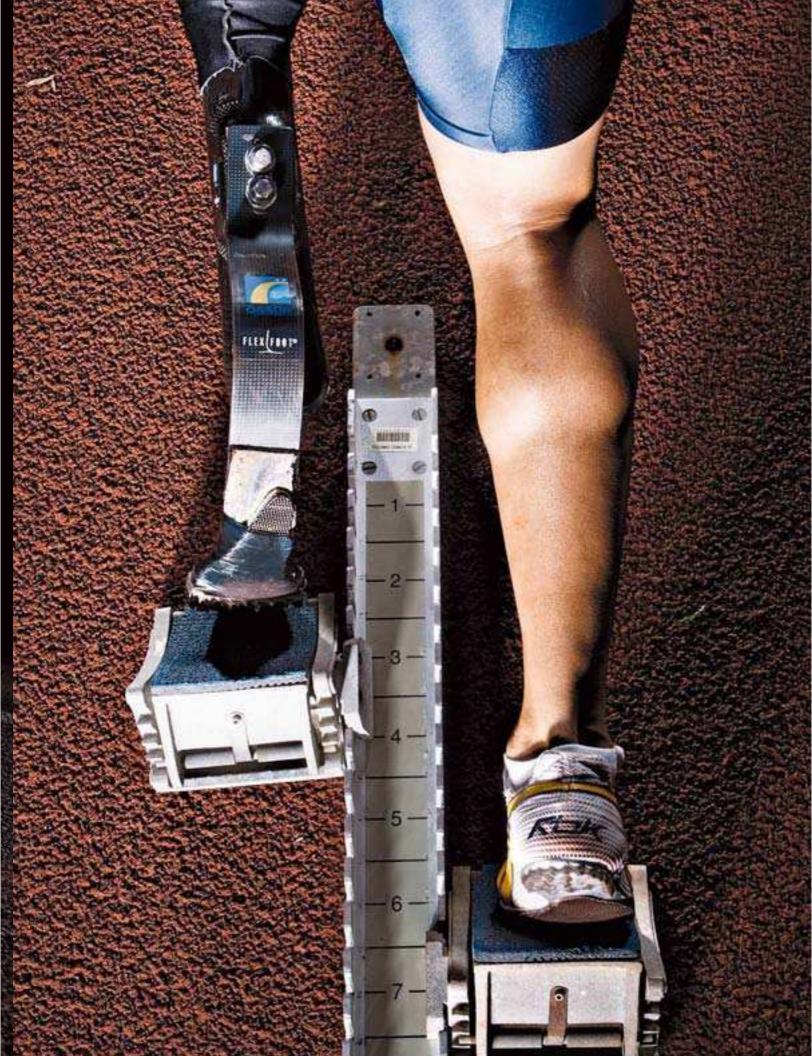














Only Kentucky matches federal SBIR-STTR Phase 1 + Phase 2 awards

Kentucky will match both Phase 1 and Phase 2 federal SBIR and STTR awards to our high-tech small businesses – no other state has a program designed to do just that.

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We are now accepting applications from companies in Kentucky (or willing to relocate to Kentucky) for state funds to match federal Small Business Innovation Research (SBIR) and Small Business Technology Transfer Research (STTR) grants. Phase 1 awards are matched up to \$100,000 and Phase 2 awards up to \$500,000 per year for two years.

Kentucky offers a wide range of support for high-tech

small businesses, including grants, tax incentives, and other forms of early-stage funding. Our statewide network of Innovation and Commercialization Centers can offer business management and entrepreneurial training, while helping find financing.

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For more information about our SBIR-STTR Matching Funds and other business support programs, visit www.ThinkKentucky.com/dci/sbir1.



Cabinet for Economic Development

For more information about the SBIR-STTR program in Kentucky, call 1-800-626-2930 or visit www.ThinkKentucky.com/dci/sbir1.



At *Technology Review*, putting together the TR35—our annual list of outstanding young innovators—is one of the best parts of the job. Selecting these 35 men and women, all under the age of 35, takes the better part of a year, from soliciting nominations to vetting them to gathering the opinions of the experts we depend on to help us choose the best of the best (see page 51 for a list of this year's judges). This year we began with more than 300 nominees. Settling on just 35 was a challenging task, one that led to lively discussions around conference tables and in hallways.

The result is an eclectic group of creative, driven people who have reimagined everything from the way we generate energy to the way we make social connections, from transporting premature babies to surfing the Web. This year, a few problems attracted the attention of more than one of our honorees: treating cancer, reducing our reliance on nonrenewable energy sources, keeping our online transactions secure and private, and bringing useful computing resources to the poor. With so many brilliant young minds on the case, we think the future may be brighter than many expect. But whether their work aims to save lives or merely to enrich them, the TR35 represents young talent at its most inspiring. —*The Editors*



Mark Zuckerberg p. 65



INNOVATOR OF THE YEAR

David Berry, 29

Flagship Ventures

Renewable petroleum from microbes

By Stephen S. Hall

avid Berry is sitting in a midtown Manhattan coffee shop, taking a break from a carbon-trading conference across the street, when a news report on the wall-mounted television catches his eye. The CNN dispatch describes how scientists have shown, in animal experiments, that Viagra might be used to alleviate symptoms of jet lag.

"It's interesting," Berry says, chuckling, as his eyes wander back to the screen. "We were talking about a year ago of using Viagra to treat jet lag." One side effect of Viagra widely reported in the medical literature has been the perception of blue light, he continues, and blue light has also been shown to reset circadian clocks in humans. "I like when I see these things actually come true," he says.

It's one thought that never went beyond a blue-sky conversation among his venture capital colleagues. But it reflects how easily ideas come to Berry, a Harvard-trained MD who earned his PhD through the Biological Engineering Division at MIT and for the past two years has been a principal in the venture capital firm Flagship Ventures in Cambridge, MA.

Since receiving his bachelor's degree from MIT in 2000, Berry has helped develop a way to treat stroke, thought up a new approach to cancer therapy, and, most recently, created a system to genetically engineer microbes to produce biofuels. He has 21 patent applications pending, and his intellectual curiosity touches on therapeutic medicine, diagnostic devices, and now, most notably, alternative energy technologies. His innovations in energy form the conceptual basis of LS9, a California-based renewable-petroleum company that has received \$5 million in venture funding from Flagship and Khosla Ventures in California (see "Better Biofuels," July/August 2007).

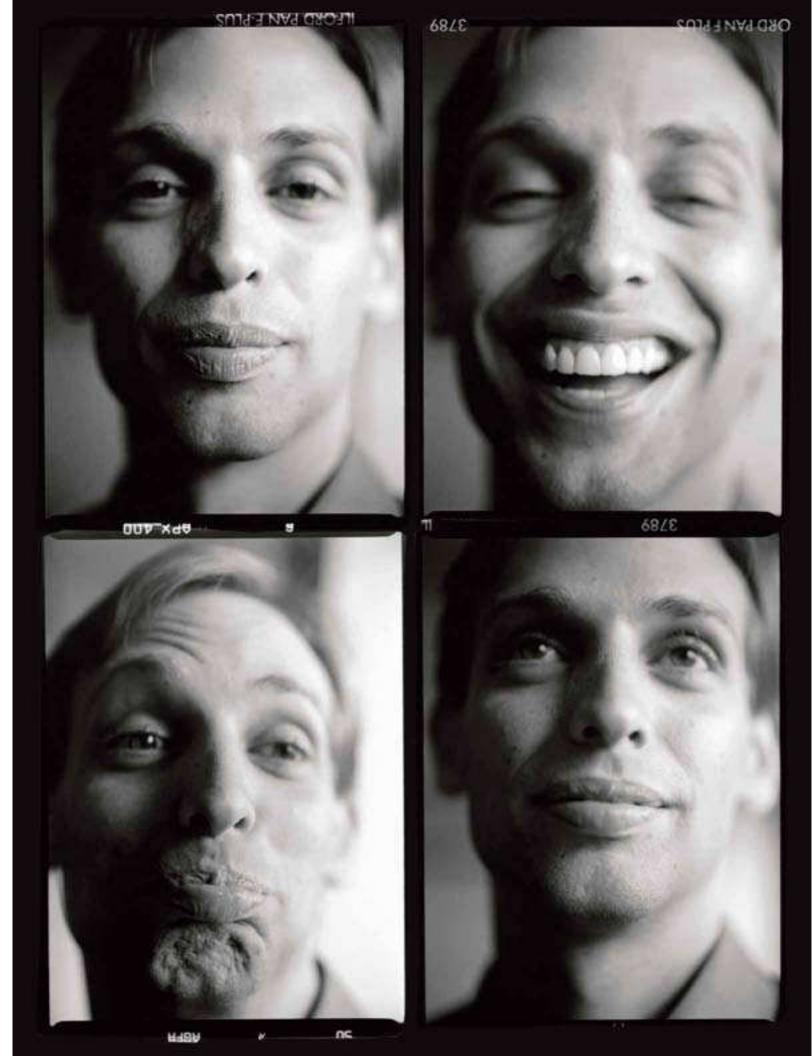
Berry points out that a number of the pioneering biotech companies were thinking about energy and biofuels, specifically ethanol, in the 1970s. "What's interesting," he says, "is that, as a field, we're making a full circle and going back to the things biotechs thought about way back then. But now we're bringing new technological tools to make the same problems more tractable."

On the first working day of each week, Flagship Ventures holds a group meeting to review investments and discuss new ideas. One day this May, David Berry was the youngest, and probably the most earnest, of about a dozen VCs gathered in Flagship's seventh-floor conference room, with its grand view of sailboats plying the Charles River. The meeting ran a little long, and Berry apologized when he finally emerged. "We were talking about a potential new idea in drug delivery," he explained. Although the details of that technology remained discreetly fuzzy, it was very clear that these are heady, palpably exciting conversations for him. "You're discussing some of the hottest, most compelling new technologies around," he says. "I'm having a blast."

Berry took a seat at that conference table with no formal training in finance but a track record in technology. In graduate school, he began tinkering with a molecule that could pass through the blood-brain barrier and showed promise as a stroke treatment. The protein, an engineered version of fibroblast growth factor 2, produced functional improvement in a test animal modeling symptoms of stroke, and it brought out in Berry another quality conducive to innovation: restlessness. Berry realized that studying the protein could lead to a PhD far more quickly than most projects, and he seized the occasion. He got his PhD in 2005 (finishing his MD a year later), and the biotech company ViaCell briefly attempted to develop the molecule as a drug.

Berry also experimented with ways to reversibly attach polymers to sugar molecules and came up with a way to kill cancer cells by binding polymers to heparin, the well-known blood thinner. Berry's polymer packaging makes cancer cells absorb heparin more quickly; once inside the cells, the heparin disrupts biochemical pathways, ultimately leading to cell death. The technology garnered the attention of Momenta Pharmaceuticals, a biotech company in Cambridge, MA; Berry garnered another publication, and another patent application.

"What makes David unusual is that there's nothing that's going to stop him," says Robert Langer, a chemical engi-



neer at MIT in whose lab Berry studied. "He has no fear. He's willing to tackle any idea, and he has lots of ideas. The breadth of his scientific curiosity and his belief in himself are pretty remarkable for somebody his age."

In 2004, Berry had no greater ambition than to run an academic lab, develop new technologies, and hustle them out into the commercial world. But then, in 2005, Flagship Ventures sought his input on a life science company it was starting. By the end of the year, that consulting job had evolved into an invitation to join the firm as a principal. In Flagship's emphasis on developing the core concepts for new companies in-house, Berry saw an irresistible opportunity to jump-start innovation by funding it at its earliest stages. Although Flagship's previous startups tended to focus on traditional life sciences like genomics, the company was increasingly interested in taking biology in a new direction: energy. "Back in 2005," Berry recalls, "we were saying, 'What would be interesting in the fuel space?" The project ended up in Berry's hands.

Berry's goal was nothing less than "to develop a novel and far-reaching solution to the energy problem." In collaboration with genomics researcher George Church of Harvard Medical School and plant biologist Chris Somerville of Stanford University, Berry and his Flagship colleagues set out to do something that had never been attempted

S APX 400

commercially: using the tools of synthetic biology to make microörganisms that produce something like petroleum. Berry assumed responsibility for proving that the infant company, dubbed LS9, could produce a biofuel that was renewable, better than corn-derived ethanol, and cost-competitive with fossil-based fuels.

Ethanol is the most common biofuel, but many observers, including Berry, have reservations about corn-based ethanol as a long-term solution to the fuel crisis. Ethanol has only about two-thirds as much intrinsic energy as petroleum, and producing it requires considerable agricultural resources.

Berry took the lead in designing a system that allowed LS9 researchers to alter the metabolic machinery of

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microörganisms, turning them into living hydrocarbon refineries. He began with biochemical pathways that microbes use to convert glucose into energy-storing molecules called fatty acids. Working with LS9 scientists, he then plucked genes from various other organisms to create a system of metabolic modules that can be inserted into microbes; in different combinations, these modules induce the microbes to produce what are, for all practical purposes, the equivalents of crude oil, diesel, gasoline, or hydrocarbon-based industrial chemicals.

Along the way, Berry and his colleagues had to soup up the activity of certain genes to increase the output of specific intermediate molecules. They also had to determine how to selectively block other metabolic pathways so that their microbes would stay focused on producing hydrocarbons. And they figured out how to make the microörganisms secrete the final product in such a way that it could easily be collected.

"David is responsible in large part for LS9's intellectualproperty real estate," says Noubar Afeyan, Flagship's CEO. "If you strip away his contributions, there's no company."

Since the technology is proprietary and still in the early stages of development, Berry won't identify the types of organisms and the specific cellular processes involved. LS9 has been optimizing its system and trying to increase the yields of its designer biofuels at its California facility. Current yields in the lab are an order of magnitude lower than those for ethanol produced from cellulose, Afeyan says, but the company hopes to reach a comparable yield within a year.



2007 TR35 Judges

Angela Belcher* Professor of materials science and engineering and of biological engineering,

Rodney Brooks Professor of robotics,

J. J. Cadiz* Program manager, Incubation Group, Microsoft Research

George Candea* Assistant professor of computer and communication sciences, École Polytechnique

Fédérale de Lausanne Yet-Ming Chiang Professor of ceramics

George Church Professor of genetics; director, Center for Computational Genetics, Harvard Medical School Vicki Colvin

Professor of chemistry and of chemical engineering; director, Center for Biological and Environmental Nanotechnology, Rice University

Miguel de Icaza' Vice president of developer platforms, Novell

Drew Endy Assistant professor of biological engineering,

Claire Gmachl* Associate professor of electrical engineering, Princeton University Irene Greif IBM Fellow; director, Collaborative User Experience Group,

IBM Watson Research

J. Karl Hedrick Professor of mechanical engineering; director, Vehicle Dynamics Lab, University of California,

Rerkele Tracey Ho* Assistant professor of electrical engineering and computer science,

Caltech **Brian Hughes** Chairman and product

engineer, HBN Shoe Guido Jouret Chief technology officer, Emerging Markets Technology Group, Cisco Systems

Thomas Keim Principal research engineer assistant director, Laboratory for Electromagnetic and Electronic Systems

Lionel Kimerling Professor of materials science and engineer ing; director, Materials Processing Center,

Vikram Sheel Kumar¹

Cofounder, chairman, and chief medical officer, Richard Lester Professor of nuclear science and engineering; director, Industrial Perfor-

mance Center, MIT Håkon Wium Lie¹ Chief technology officer, Opera Software

Cherry Murray
Deputy director for science
and technology, Lawrence Livermore National Laboratory

Stephen Quake* Professor of

bioengineering, Stanford University

Dipankar Raychaudhuri Professor of electrical and computer engineering; director, Winlab, Rutaers University

Mark Reed
Professor of engineering and applied science; associate director, Yale Institute for Nanoscience and Quantum Engineering, Yale University

Carmichael Roberts* Cofounder and CEO, WMR Riomedical Joshua Schachter* Founder

Del.icio.u Bjarne Stroustrup Professor of computer science, Texas A&M University

Sophie Vandebroek Chief technology officer; president, Xerox Innovation Group,

David Victor Professor of law: director. Program on Energy and Sustainable Development, Stanford University Jimmy Wales Founder, Wikipedia; cofounder, Wikia

Jennifer West* bioengineering, Rice University Adjunct professor of mechanical engineering, Carnegie Mellon University; chairman, Pittsburgh Electric

*Past TR100/TR35 honoree

Engines

Nonetheless, LS9 has no products so far and many hurdles to surmount. Berry's system, for example, is designed to exploit glucose-based feedstocks such as cellulose. Berry says he is "agnostic" about what source of cellulose might drive the LS9 system on an industrial scale; he lists switchgrass, wood chips, poplar trees, and Miscanthus, a tall grass similar to sugarcane, as potential sources of biomass. But a costeffective and efficient source of cellulose is one of the more significant bottlenecks in the production of any biofuel.

Despite these uncertainties, Berry's method offers many of the advantages of biofuels in general. The raw feedstock would be agricultural and homegrown; it would be renewable; and it would, in principle, provide a more environmentally friendly source of energy than traditional crude oil (which requires smoke-belching refineries). With microbes doing all the work, fuels could be produced in large fermentation tanks of the sort used by biotech companies.

The biological synthesis of hydrocarbons is "a technology with really game-changing potential," Berry says. "It has security benefits. It has sustainability benefits. And the value of that, on top of a cost benefit, makes it a very compelling technology." And one of the most compelling parts of the story behind that technology is that it was developed by a doctor in his 20s. TR



NANOTECHNOLOGY

Abraham Stroock, 34

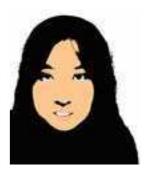
Cornell University Microfluidic biomaterials

When Abraham Stroock looks at a tree, he sees a complex feat of engineering. Inside the trunk, the branches, and the leaves, an intricate network of capillaries draws water dozens of meters into the air, with nary a pump in sight. This incredible system inspires Stroock's approach to microfluidics.

Microfluidics involves moving tiny volumes of liquid through channels that are usually etched into a rigid material such as glass or silicon. Stroock, however, works with hydrogels, soft polymers that absorb water. Recently, he molded a capillary system that mimics a tree's into a slab of hydrogel. This "synthetic tree" uses evaporation to pull water through its capillaries. The force it achieves is equivalent to that required to move liquid up a vertical column 85 meters high—the height of a redwood.

Liquid diffuses out of the hydrogel capillaries and into the surrounding material, just as it would in living tissue. Hydrogels are also biologically compatible, so such systems could serve as wound dressings that remove fluid and deliver drugs to promote healing. They could also

act as three-dimensional scaffolds for engineered tissues; oxygen and nutrients could travel to cells inside the scaffolds. To mimic real tissues, the materials will ultimately have to provide conduits for proteins and cells—another step in Stroock's plan to "give the material life". - Corinna Wu



BIOTECHNOLOGY

Doris Tsao, 31

University of Bremen (Germany)

Shedding light on how our brains recognize faces

Glance at a newsmagazine and you probably recognize the face on the cover right away-Al Gore looking serious in profile, or perhaps a smirking Dick Cheney. But in that instant, your brain performs a lot of complex computations: identifying the object as a face (regardless of size or viewing angle), interpreting its expression, and accessing memory to determine whether it's familiar.

Little is known about how the brain does all that, but Doris Tsao aims to unravel the process by combining two of the most important tools in neuroscience: brain imaging and electrical recordings from single neurons.

Last year, Tsao used functional magnetic resonance imaging, a technology that indirectly measures brain

JUSTIN WOOD

activity, to identify areas of the monkey brain that are active only when the animals look at faces. She then used a detailed MRI picture to guide an electrode to several of those spots. Using the electrode to record activity from individual neurons, she found that different cells respond to different facial characteristics—say, the shape of the face or the size of the eyes. This exquisite level of detail would have been impossible with imaging alone.

Tsao's work yields important clues to how neural activity leads to conscious visual perception, says Christof Koch, a neuroscientist at Caltech. "It's a step toward answering the age-old question 'What is the relation between the mind and the brain?" —Emily Singer



TELECOM

Sanjit Biswas, 25

Meraki Networks

Cheap, easy Internet access

As a side project when he was a graduate student at MIT, Sanjit Biswas worked on a system for connecting local residents to the Internet wirelessly. In 2006, a nonprofit group asked if the technology could help provide Internet service to the poor. Intrigued, Biswas took a leave of absence to cofound



INTERNET

Kevin Rose, 30

Digg

Online social bookmarking

In 2004, Kevin Rose set out to transform the way people read news. The result, Digg, mixes blogging, online syndication, social networking, and "crowdsourcing"-which combines the knowledge and opinions of many individuals-to create an online newspaper of stories selected by the masses. The principles behind Digg are simple. Users can submit stories; if other users like a story, they can "digg," or praise, it; if not, they can "bury," or condemn, it. A new visitor sees a ceaseless scroll of stories accompanied by a flurry of comments. Digg's straightforward rules have made it hugely popular: less than three years after its launch, more than 17 million users visit the site each month. But with success, Digg has also attracted controversy. Some observers decry the inanity of the site's top stories, and even habitual users admit that the comments are mostly puerile. Rose, who acts as the site's chief architect, must increasingly weigh the anarchic free speech that characterized Digg's early days against a more responsible approach to publishing that protects intellectual property and other institutional interests.

TR: Digg is a testament to collective wisdom—but I wonder if at any point you've felt embarrassed, either by the top stories or by the comments about the stories.

Kevin Rose: Not really. Every single day I find something that's really interesting that I wouldn't have found on a traditional news outlet, an interesting nugget of information that happens to surface on an unknown blog or a website that I haven't heard of before. I think if you go on CNN.com or MSNBC.com, you're going to find the news that you're used to reading. When you come to Digg, you never know what you're going to get. What about the common criticism of Digg, that what tends to be "dugg" is often superficial? Are the most popular stories on Digg really the best stories?

As we speak, right now, the top three stories on Digg are doit-yourself lucid dreaming, an update about the Apple iPhone, and why a former official of the Reagan administration thinks that President Bush should be tried as a war criminal. We get a mixture of all types of news on our front page.

continued on page 55

Meraki Networks in Mountain View, CA, and create wireless mesh networks that would link people to the Internet cheaply.

In most mesh networks, all the nodes that receive a particular data packet forward it on; but in Biswas's version, the nodes "talk" to each other and decide, on the basis of the packet's destination and their own signal strengths, which one of them should forward it. The protocol also takes into account changing network conditions, as users sign on or off, or, say, a passing truck blocks a node's radio signal. Biswas's protocol, combined with commonly available hardware components, allows Meraki to produce Wi-Fi routers that cost as little as \$50. (The routers Biswas used at MIT initially cost \$1,500.)

Here's how a Meraki network works: a user plugs a router into a broadband Internet connection; that person's neighbors stick routers to their windows, and a mesh network of up to hundreds of people forms automatically. Users can give away or sell Internet access to their neighbors. There are already Meraki-based networks in 25 countries, from Slovakia to Venezuela, serving more than 15,000 users. —Neil Savage

NANOTECHNOLOGY

Erik Bakkers, 34

Philips Research Laboratories

Combining semiconductors

Silicon chips have revolutionized electronics, but for certain purposes, such as radio frequency transmission, chips made from compound semiconductors like gallium arse-





nide or indium phosphide work much better. Erik Bakkers of Philips Research Laboratories in Eindhoven, the Netherlands, has found a way to mix semiconductors on a single chip.

Different semiconductors are normally incompatible, partly because they expand at different rates when heated. Combining them thus leads to physical strain that reduces performance. Bakkers solved the problem by building circuits out of nanowires. Because the point of contact between the different semiconductors is small—just a few tens of nanometers—there is no strain.

To grow a nanowire, Bakkers places a gold nanoparticle on top of a silicon wafer. Then he exposes the wafer to a vapor of, say, gallium arsenide; the nanoparticle catalyzes the growth of a gallium arsenide nanowire.

This technique opens up possibilities for multipurpose chips that could be used in wireless devices and other applications. It could also make it easier for engineers to take advantage of the inherent properties of compound semiconductors to create highly efficient LEDs, faster transistors, optical interconnects to rapidly shunt data around chips, or fast, highly sensitive biosensors to detect diseases.

-Neil Savage

MEDICINE

Shetal Shah, 32

State University of New York, Stony Brook Cushioning preemies

As a fellow in neonatology, Shetal Shah spent hundreds of hours jouncing around in ambulances, transporting dangerously ill premature babies to New York University Medical Center's specialized neonatal unit. "You have a lot of time to think when you're sitting there," he says. "I noticed how disruptive these vibrations were to me, and I started thinking, Well, what does it mean for the infant?" Shah, now an assistant professor of pediatrics at SUNY Stony Brook, knew that

preemies who have to be transferred between hospitals tend to have more problems than those who don't-problems that include bleeding in the brain and chronic lung disease. So he set about finding out what role those jolts might play. He adapted an accelerometer, attached it to the head of a neonatal mannequin, and drove around the city in a borrowed ambulance. This gave him approximate measurements of the forces a transported baby experiences every minute. To damp those forces, Shah initially used a free sample of memory foam from a mattress store but eventually developed a patent-pending transport system. Some companies have expressed interest, and the military is studying its potential to help protect soldiers with head trauma. -Erika Jonietz





TELECOM

Jeff LaPorte, 30

Ego Communications

Internet-based calling from mobile phones

PROBLEM: If you're at your computer, you can use Skype and similar programs to make zero-cost domestic and international phone calls. But if you're forced to use your mobile phone for an international call, you pay exorbitant rates. Sending mobile calls over the Internet, as Skype does with PC calls, would be cheaper—but the big carriers don't offer such a service, and their clout with handset manufacturers makes it hard for third-party developers to create easy-to-use Internet calling software.

SOLUTION: Jeff LaPorte conceived a clever end run around the wireless carriers and cofounded Eqo Communications of Vancouver, British Colum-



bia, to market the idea. When an Eqo (pronounced "echo") user dials an international number, software downloaded to the phone actually connects the call

to a local Ego number. From there, an Ego server converts the user's voice into data packets and sends them over the Internet to an Eqo server in the destination country, which puts the call back onto the wireless voice network. There are no complicated settings to configure or 800 numbers to dial, and calls sound as good as they do with standard wireless technology. Calls from one Ego member to another are free, and other international calls can cost as little as 5 percent of what the major carriers charge. Eqo members must still have domestic wireless calling plans-but in LaPorte's words, Ego effectively "turns your local minutes into international minutes." -Wade Roush

SOFTWARE

Ivan Krstić, 21

One Laptop per Child

Making antivirus software obsolete

activities to the extreme. Born in Croatia, he received a scholarship to attend a Michigan high school when he was 13. While there, he wrote software to interpret data for a neuroscientist at the University of Michigan. He also spent two summers in Croatia, building a patient-management computer system for Zagreb Children's Hospital. He enrolled at Harvard in 2004 but then took a year's leave to return to Croatia and reëngineer the Zagreb hos-

pital's IT system—after a month-long detour to Silicon Valley to help scale up Facebook's software architecture.

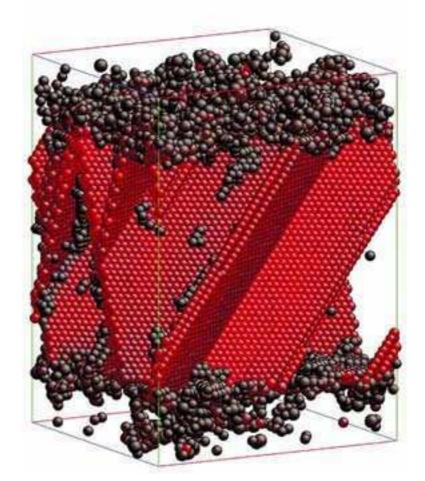
Krstić returned to Harvard in 2005 to work on a degree in computer science and theoretical math, but he took another leave last spring to become director of security architecture for the One Laptop per Child (OLPC) program, which is building inexpensive laptops for Third World children. His mandate was to create a secure system that children could use, and that



wouldn't need the tech support and continual updates that current antivirus programs require.

So he set about making such software obsolete, building into OLPC's Linux-based operating system a security platform called Bitfrost, named after Bifröst, a bridge in Norse mythology that reaches from Earth to heaven and that intruders can't cross. Instead of blocking specific viruses, the system sequesters every program on the computer in a separate virtual operating system, preventing any program from damaging the computer, stealing files, or spying on the user. Viruses are left isolated and impotent, unable to execute their code. "This defeats the entire purpose of writing a virus," says Krstić.

Some in the Linux community are so impressed with this novel approach to fighting malicious code that they have proposed making it part of the Linux standard. But since Bitfrost will allow only programs that are aware of it to run, it would make Linux incompatible with existing applications. The solution is for programmers to create "wrappers," small programs tacked onto existing applications to enable them to communicate with Bitfrost. After OLPC's computer ships late this year, Krstić plans to return to Harvardand to help write those wrappers. It's just one more extracurricular activity to take on. -Richard L. Brandt



NANOTECHNOLOGY

Ju Li, 32

Ohio State University Modeling designer materials

Researchers have long hoped that computer simulations of how atoms interact would allow them to design useful new materials from scratch. But the physics of atomic interactions rapidly becomes so complex that using it to predict the

properties and performance of real-world materials has proved extremely difficult. Ju Li. an assistant professor of materials science and engineering, has developed new algorithms to model some of the hardest-tounderstand phenomena in his field: the mechanical properties of complex, nanostructured materials. In one model. illustrated above. Li shows that combining nanoscale layers of amorphous copper zirconium and crystalline copper yields a material as much as ten times

as strong as copper, without making it too brittle to be useful. In the crystalline region in the middle, atoms in one plane slip by atoms in neighboring planes, allowing the material to easily change shape under stress. The outer amorphous layers don't change shape that way, so they keep the planes from slipping too far. Li's collaborators have already shown experimentally that this structure results in a strong but malleable material.

-Kevin Bullis

KEVIN ROSE

continued from page 52

Stories appear and disappear on Digg's main pages with tremendous speed. Does Digg move too quickly for most people to usefully understand what's there?

We try to make sure there isn't too much information flowing through the system. We are constantly tweaking our promotion algorithm to make sure that it doesn't become overwhelming. As we grow, we also have to continue to raise the bar required for stories to get promoted to the front page. One of the things that

I'm really focused on is improving the experience that's off the front page. Already you can get recommendations from friends; soon the system will start recommending stories that you might have missed or that you might find interesting, based on what you've dugg in the past. You had a small scandal recently, when you published the encryption key that protects high-definition video discs (HD-DVD). First, under industry pressure, you took down the post; then, under pressure from your users, you put it back. What is your policy on censorship?

We sort of take everything on a case-by-case basis. Things that are very clear violations of our terms of service come off the site; we don't allow pornography or pirated software, for instance. But when it's in one of the gray areas, it gets tricky.

I'm curious about your feelings about the power of the Digg community. Do you think it can be controlled or directed?

It resists being directed, that's for sure. It was very clear when the HD-DVD story broke, and then again, during the aftermath. I was watching the Digg com-

munity saying, "You can't censor us; this is free speech." The home page reflected those comments, and there was really nothing that we could do. We just built the platform. It's really up to the users to determine what they want to see on the front page. You're saying that even if you wanted to, you couldn't control what appears on Digg—except by removing a story ex post facto.

Yeah. Behind the scenes, what you don't see is that we have these servers that are just going crazy. I mean, you have thou-

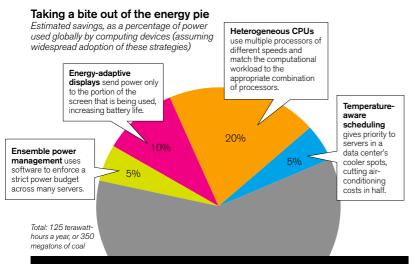
continued on page 56

Partha Ranganathan, 34

Hewlett-Packard Labs

Power-aware computing systems

Every year, computing devices—from cell phones to servers—consume at least 125 terawatt-hours of electricity, roughly the amount produced by burning 350 million tons of coal. Partha Ranganathan, principal research scientist at Hewlett-Packard Labs, is developing strategies to bring that figure down (see below). "All the ideas are very intuitive," he says. "But we needed to solve some hard problems to get there." Technologies he helped develop, which could save money and lower greenhouse-gas emissions, are already starting to appear in consumer and business products. —David Talbot



KEVIN ROSE

continued from page 55

sands and thousands of people digging stories and submitting stories and commenting and posting-and we can't write code that would keep up with that. The HD-DVD business was absolutely fascinating. I sat there, and I was kind of in shock and spellbound at the same time. It was quite the evening. Digg watchers say that 100 users are responsible for more than half the stories on the site's home page, a phenomenon that creates the potential for abuse. How do you know when someone is gaming Digg? And what can the company do to stop them?

The system knows. Our main job is to evolve the platform so that it promotes to the front page news and videos that have a diverse crowd of people digging them. We have to make sure that when a story does make the front page, it was actually chosen by individuals who wanted to see it on the front page—and not spammers trying to promote their own stories.

Have you heard that media companies are ambivalent about the traffic Digg sends them? It's hard to sell it to advertisers, because it's unpredictable, and the quality of the audience isn't measurable.

I think that's probably true. But I find it a little hard to think of Digg as a source of traffic; it was designed as just a way for people to share things with their friends. Also, this trend is much bigger than us. If a story is popular, it's going to spread. We often see a chain reaction occur: a story will hit Del.icio.us. and then it's on Digg, and then it's on Boing Boing. To date, Digg has been a haven for science and technology geeks. Can you imagine a day when Digg will truly be a general-interest site?

Definitely. Politics is one of our most popular sections and will soon overtake technology. We started off with a large tech base; we were 100 percent technology for the first year, so that's our roots. But we're quickly expanding beyond that.

-Jason Pontin

BIOTECHNOLOGY

Kristala Jones Prather, 34

MIT

Reverse-engineering biology

Scientists are increasingly looking for ways to make compounds using biological processes rather than chemical reactions. Such techniques could provide environmentally cleaner ways to manufacture everything from biofuels to drugs, avoiding the harsh solvents and toxic by-products associated with more conventional synthesis. Kristala Jones Prather, an assistant professor of chemical engineering, is developing a promising strategy for synthesizing commercial molecules biologically, from start to finish.

Organic chemists often begin with the structure of a molecule they want to make, then look for the simplest pathway of precursors to produce it. The strategy is called retrosynthesis. Prather believes that biologists can use similar reverse-engineering principles—she calls it "retrobiosynthesis"—to build compounds, stringing natural and engineered enzymes together in novel combinations inside microbial hosts such as *E. coli*.

"What I'm interested in is designing organisms to be chemical factories," says Prather, who spent four years in the Bioprocess Research and Development department at Merck. "We used biological systems to do one reaction, and we passed that back to a group of chemists who would do the rest of the fun stuff, and I started thinking, 'Why can't biology do more?""

In 2004, Prather left industry and joined academia so she could help biology do more. Enzymes catalyze a wide range of chemical reactions. Prather is developing a database of these reactions; it includes algorithms that will identify the enzymes most useful for constructing novel metabolic pathways—in many cases leading to chemicals that are not produced through any natural biosynthetic pathway.

AND COLOW (TRAINER)







INTERNET

Anna Lysyanskaya, 31

Securing online privacy

PROBLEM: People want to use the Internet without having their habits documented or their personal data stolen. But they need to prove they're authorized to access bank accounts or subscription sites, processes that usually involve revealing their identities.

SOLUTION: Anna Lysyanskaya, an assistant professor of computer science, has developed a practical way for people to securely log in to websites without providing any identifying information. Her approach relies on "zero-knowledge proofs." Say you want to browse a newspaper's archives in total privacy. With zero-

knowledge proofs, you subscribe using a pseudonym and receive digitally signed credentials. When you access the paper's site, your computer sends



encrypted versions of the pseudonym and credentials. The archive can't decrypt this information; instead, it tests it for characteristics that valid data must have. (A certain field has to contain a specific number of digits, for example.) If the credentials are fake, some attribute will be wrong, and the site will be able to tell.

Zero-knowledge proofs have been around for a while, but they've required too much computing power to be practical. Collaborating with Jan Camenisch of the IBM Zürich Research Laboratory, Lysyanskaya developed algorithms that make both generating and testing credentials much more efficient. IBM is incorporating these algorithms into its Idemix anonymouscredential systems. -Neil Savage

When multiple enzymes might fit the bill, her software will help select the best one; when no appropriate enzyme is known, the program will help determine which existing enzyme should be modified in order to fill the hole. Prather's software should be a boon to other synthetic biologists who now construct metabolic pathways by painstakingly combing the literature for possible enzymes, says Jay Keasling, a leading synthetic biologist at the University of California, Berkeley, who supervised her PhD thesis.

Adds John Woodley, professor of chemical engineering at the Technical University of Denmark, "It's a very clever idea." - Jennifer Chu





NANOTECHNOLOGY

Adam Cohen, 28

Harvard University
Making molecules motionless

ow do you get a molecule to stop jiggling long enough to get a good look at it? It's a problem that has vexed biologists for years. But Adam Cohen, who worked on it for the last four years as a graduate student at Stanford University, has solved it.

Tiny objects, such as cells, viruses, and proteins, naturally flitter about in solution. It's called Brownian motion, and Albert Einstein explained it more than a century ago: particles in solution are invisibly bumped by water molecules. Researchers have been largely powerless to stop the jiggling of particles smaller than 100 nanometers, making it difficult to directly observe, for example, a single protein in its natural environment.

By developing a method for gently stopping the motion of nanoparticles, Cohen has given scientists a way to more easily discern differences between individual molecules and determine how those differences affect biological processes. Cohen points out that biological molecules like proteins exhibit "lots of variability." That variability—say, how an odd protein is misshaped—can have important medical implications.

Optical tweezers, invented in the mid-1980s, use lasers to trap objects in solution by exerting a force on them. This technique works well with objects larger than 100 nanometers, but Cohen knew that a laser trained on something as small as a protein would "cook it rather than trap it." So he turned to electrokinetic forces.

Cohen traps his molecules using a microfluidic chamber lined with electrodes. The microfluidic device is mounted under a standard fluorescence microscope that sends images of the targeted nanoparticle to a PC, which quickly determines the exact location of the molecule and applies voltages to the tiny chamber. These precisely calibrated voltages create minuscule drifts in the fluid that cancel out the Brownian motion of the molecule. "It's like balancing a broom pole on your palm," Cohen explains. "If you keep adjusting your palm, you can keep it balanced."

Cohen begins work as an assistant professor of physical chemistry at Harvard University this fall. Now that his instrument works, he says, he is anticipating "the real excitement of making measurements on biological molecules." —David Rotman



INTERNET

Tadayoshi Kohno, 29

University of Washington Securing systems cryptographically

Our reliance on the Internet is increasing all the time. Tadayoshi Kohno, an assistant professor of computer science and engineering, worries that even if our data is encrypted, hackers can still glean information about us by working around the codes. For instance, someone tapping into your system might not be able to view the movie you're watching but could guess its title from properties such as the file size and the compression algorithm used.

So Kohno invented the concept of systems-oriented provable security. Traditionally, cryptologists have assumed that a security protocol is unbreakable if no one they show it to can crack it. But with provable security, they use sophisticated math to show that cracking a given code would require someone to decipher a cryptographic "building block" that's known to be secure.

Kohno extended this technique to the system level, examining everything from the software that compresses a file to the Internet protocols



used to send it. He searches for weak points that might leak identifying information and writes provably secure algorithms to protect them. One of his schemes can handle data transmitted at 10 gigabits per second, the new Internet standard—a rate that overwhelmed previous security protocols. The U.S. government is incorporating a derivative of the scheme into an official encryption standard; Kohno anticipates that banks and corporate networks will use it as well. -Neil Savage

INTERNET

Tariq Krim, 34

Netvibes
Building a personal,
dynamic Web page

"When I open my Web browser, I want to get the latest stuff that's really important to me," says software engineer, Web entrepreneur, and former journalist Tariq Krim. That's the idea behind Netvibes, a free and "agnostic" Web service Krim created to let netizens build customized pages from disparate modules such as RSS feeds from blogs, competing news sites such as Google and Yahoo, and even user-translated international sites. On the "Tariq" tab of his own Netvibes page (right), Krim uses search modules to track what bloggers are saying about him and his company. -Wade Roush



BIOTECHNOLOGY

J. Christopher Anderson, 31

University of California, Berkeley Creating tumor-killing bacteria

Using the engineering approach of synthetic biology, Chris Anderson has set out to program bacteria to selectively kill cancer cells. He is combining DNA sequences from different types of bacteria and inserting them into the bacterium *E. coli* to create an organism that can evade the immune system, home in on tumors, and trick cancer cells into letting it inside, where it releases a toxin.

Anderson has built and tested all the biological parts for the cancerkilling bug and is now working on putting them together. "All of these things exist as little genetic programs," he says. He also expects to be able to engineer bacteria for other medical purposes, because "everything is designed in a modular way, so the parts can be used for a totally different application that shares some of the same problems." For example, the genetic parts he has developed could be used to deliver medicine to an HIV-infected immune cell. —Emily Singer

2) When they detect the low-oxygen environment of a tumor, the bacteria produce invasin, a protein that allows them to infiltrate the cancer cells

Engineered bacteria are injected into the blood-stream; polysaccharide molecules on their surfaces allow them to evade the immune system

3) The invasin binds to the cancer cells, prompting the cells to engulf the bacteria

Invasin

Chromosome: The genetic parts of the cancer-fighting system are integrated into the

Tumor-killing *E. coli*

4) The cancer cell bursts the bacterium, releasing a toxic enzyme that kills the cell







ENERGY

Javier García-Martínez, 34

University of Alicante (Spain) New zeolites for cracking petroleum

PROBLEM: Turning crude oil into gasoline involves a process known as catalytic cracking, which splits large hydrocarbon molecules into simpler fragments. Refineries traditionally use synthetic porous materials called zeolites as catalysts for these reactions.

The standard zeolite has pores less than one nanometer across, so the largest hydrocarbon molecules can't fit inside them and undergo the reactions that break the bonds between atoms. Increasing the pore size of the zeolites would allow a larger fraction of crude

oil to be converted into useful products. Companies have spent three decades and millions of dollars trying to increase pore size, without much success.



SOLUTION: Javier García-Martínez, leader of the Molecular Nanotechnology Lab at the University of Alicante in Spain, has developed a way to increase pore size to between two and ten nanometers, the ideal range for producing gasoline. He mixes zeolites with an alkaline solution. A soaplike surfactant is added to the solution and forms small structures that the zeolites reconstruct themselves around. The surfactant is then burned off.

Choosing surfactants of different molecular sizes allows García-Martínez to tune the pore size, so he can optimize the zeolites for other purposes, such as chemical synthesis or water treatment. He cofounded a company, Rive Technology, that is now working to commercialize the technology and test it in a working refinery. —Corinna Wu

INTERNET

Luis von Ahn, 29

Carnegie Mellon University
Using "captchas" to digitize books

uis von Ahn is a pioneer of "captchas"-those strings of distorted characters that websites force you to recognize and type in order to establish that you are a person and not a malevolent computer. But he finds the technology's success a mixed blessing. "At first I was feeling quite proud of myself," says von Ahn, a 2006 MacArthur "genius grant" recipient who created captchas (an acronym for "completely automated public Turing test to tell computers and humans apart") for Yahoo in 2000 to thwart automated e-mail account registration, a tool of spammers. "But then I was feeling bad, because every time you solve a captcha, you waste 10 seconds." People around the world solve an estimated 60 million captchas every day, adding up to more than 150,000 wasted hours.

Von Ahn, an assistant professor of computer science, is a leader in using human skills to make computers work better. For example, he created an online game in which players identify elements in photographs; their answers help improve image-search algorithms. He's now trying to put captchas to work in one of the epic efforts of the information age: digitizing millions of old books and making them searchable online.

An estimated 8 percent of words in these old books can't be read by the optical character recognition (OCR) software used to scan them. Von Ahn has teamed with the nonprofit Internet Archive to use captchas to help interpret those words. After all, he says, "while you are solving a captcha, you are solving a task that computers can't perform." So he created a tool, called "recaptcha," that pairs an unknown word with a known one. He distorts them both and puts a line through them-standard techniques for creating captchas. A user must decipher both captchas to access a site. The accurate typing of the known word serves the security purpose of captchas and adds a measure of confidence that the unknown word was identified correctly and can be used in place of the OCR's gibberish. Volunteers have begun deploying recaptchas, and the technique has been used to decipher two million words for the Internet Archive's book digitization effort. Recaptchas tap the joint power of people, networks, and computers in a way that should have a big impact, says Brewster Kahle, an Internet entrepreneur and cofounder of the archive: "It is like an army of ants building the Taj Mahal." – David Talbot





HUMANITARIAN OF THE YEAR

Tapan Parikh, 33

University of Washington
Simple, powerful mobile tools for developing economies
By James Surowiecki

hen fishermen from the Indian state of Kerala are done fishing each day, they have to decide which of an array of ports they should sail for in order to sell their catch. Traditionally, the fishermen have made the decision at random—or, to put it more charitably, by instinct. Then they got mobile phones. That allowed them to call each port and discover where different fishes were poorly stocked, and therefore where they would be likely to get the best price for their goods. That helped the fishermen reap a profit, but it also meant that instead of one port's being stuck with more fish than could be sold while other ports ran short, there was a better chance that supply would be closer to demand at all the ports. The fishermen became more productive, markets became more efficient, and the Keralan economy as a whole got stronger.

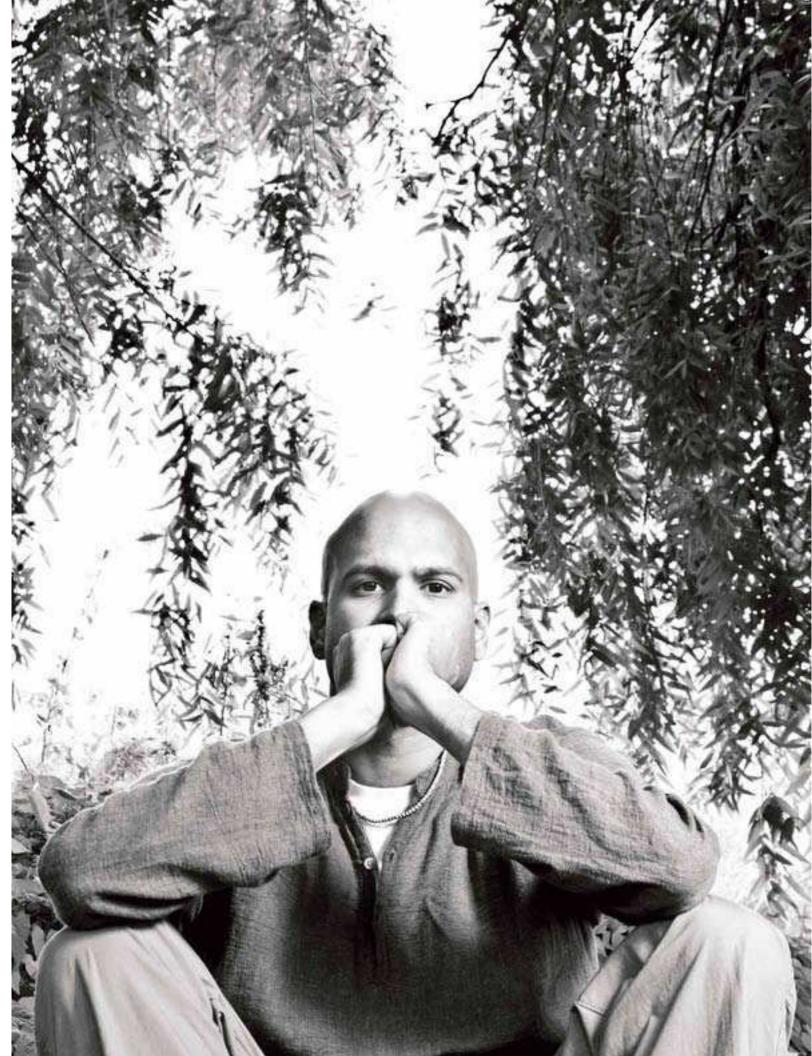
This story demonstrates an easily forgotten idea: relatively simple improvements in information and communication technologies can have a dramatic effect on the way businesses and markets work. That idea is central to the work of Tapan Parikh, a doctoral student in computer science and the founder of a company called Ekgaon Technologies. Parikh has created information systems tailored for small-business people in the developing world systems with the mobile phone, rather than the PC, at their core. His goal is to make it easier for these business owners to manage their own operations in an efficient and transparent way, and to build connections both with established financial institutions and with consumers in the developed world. This will help them-they'll be able to get money to expand their operations and, ideally, find better prices for what they sell-and it should be a boon to development as well.

In the developing world, working with mobile phones has obvious advantages: they're ubiquitous even in poorer countries (there are 185 million cell-phone subscribers in India and more than 200 million in Africa); they're relatively affordable; and with the right software, they're easy to use. So Parikh developed Cam (so called because the phone's

camera plays a key role in the user interface), a toolkit that makes it simple to use phones to capture images and scan documents, enter and process data, and run interactive audio and video. The Keralan fishermen had been able to improve their business simply by making phone calls. Cam would carry the process a step further, by taking advantage of modern phones' computing capabilities.

Parikh's most important project with Cam has focused on perhaps the trendiest field in economic development: microfinance, in which lending groups grant tiny loans—on the order of \$25-to people in the developing world, usually to fund small-business ventures. (Muhammad Yunus, the founder of the best-known microfinance institution, the Grameen Bank, won the Nobel Peace Prize last year for his work in establishing the field.) The best-publicized version of microfinance involves a solo entrepreneur getting a small loan from a well-financed bank. But Parikh is collaborating with organizations that are more representative of the way it usually works. A big chunk of the microfinance business in India, for example, is conducted by self-help groups, in which 15 to 20 people (usually women) pool their capital and then meet weekly or monthly to make collective decisions about loans to members of the group. They also use their collective borrowing power to obtain loans from nongovernmental aid organizations or from financial institutions, and then lend that money to their members.

Parikh built a software system on top of Cam to assist self-help groups in managing their information and their operations. Unglamorously called SHG MIS (for "self-help group management and information system"), it includes a Cam-based application for entering and processing data, a text-messaging tool for uploading data to online databases, and a package of Web-based software for managing data and reporting it to any institution that has lent money to the self-help group. Such groups have traditionally relied on paper documentation, however, and because their members still trust paper, the software also includes a bar-code-based system. Loan applications, grants, receipts, and other docu-



ments are printed with identifying bar codes; the software enables the phone to scan the code, identify the document, photograph it, process the data it contains, and associate that data with the code. The result is a system that facilitates a quick and accurate flow of data from small villages to bigger cities, and vice versa.

In addition to providing a more efficient way for selfhelp groups to manage their finances, SHG MIS allows such groups to overcome two major challenges. First, it enables them to run their internal operations in a fair and transparent way, while ensuring that their loans make economic sense.

Parikh's invention

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"In these groups, things are often done in a somewhat ad hoc manner, using informal documentation," Parikh says, "which can lead to instability and impermanence and contribute to the kinds of tensions that lead small groups to fall apart." His software gives groups a more systematic method of documenting decisions, tracking financial performance over time, and collecting information on which kinds of loans work and which don't. These advantages should help groups make better decisions and reduce internal political tensions.

The software could also improve the flow of information between self-help groups and the formal financial sector, which

should enable them to get capital at better rates. As things stand right now, Parikh says, bankers' interest in microfinance is so high that the supply of capital more than meets demand. But because it's difficult to track so many small, scattered loans, banks tend to offer the same deal to every business, regardless of performance, ability to repay, and so on. If self-help groups could document their performance in a formal, auditable system that banks could access quickly and reliably, the groups would be more likely to get fair prices. They would have access to more capital, too.

Two things are striking about Parikh's invention. The first is how unremarkable it seems, and yet how consequential it is in practice. Parikh did not radically reimagine computing, nor did he make a major break with the way financial data is managed in the developed world. Instead, he focused on something whose benefits we take for granted—reliable, instant access to financial data—and figured out an easy, affordable way to bring it to people who need it. The second thing is that instead of forcing small-business people to discard all their old ways and embrace an entirely new

paradigm, Parikh's work attempts to meet them, as it were, where they live, in order to enhance their existing abilities and resources. Other engineers might insist that the self-help groups need to do away with paper, since it's less efficient than simply using digital entry devices, or develop PC-centered systems, since mobile phones (whatever their virtues) are limited in their power and capacity. Cam, though, relies on a different strategy, one that emerges from the bottom rather than being imposed from the top.

This strategy runs counter to the way computer science has traditionally been done. Many computer scientists tend

to think more about making machines faster and more powerful than they do about making sure they meet people's needs. What's distinctive about Parikh's approach is that he's spent so much of the past seven years working not in front of a computer but in the field, talking with the people he hopes will eventually be his customers. It's a way of life that seems more characteristic of an anthropologist than a coder, but it's responsible for much of what Cam has become. In fact, Parikh says, "all of my ideas are really just rehashes of ideas that local people have come up with."

Parikh has adopted the same approach in his work with fair-trade coffee farmers in Guatemala. In recent years, the "fair trade" and "organic" designations have come to have real economic value: fairtrade farmers are guaranteed a minimum price for their crop, and organic farmers

can often charge higher prices. But these labels also cause problems. Because they're one-size-fits-all, they reduce the incentive for farmers to improve their growing methods or the quality of their crops above the general minimum. And they create incentives for cheating, which in turn reduces the value of the label to consumers: are you really sure how that organic coffee you bought at Starbucks or Peet's was grown? So Parikh devised a Cam system called Randi, for "representation and inspection tool." It allows farm inspectors to use mobile phones to systematically photograph and document farms in order to ensure their compliance with quality and production standards, and to put that data online so that it's easily found by certifying agencies, whole-salers, and consumers.

In other words, if you wanted to know how that organic coffee was grown and whether a fair price was paid for it, Randi would let you find out. In the long run, the system would allow today's simple labels to become more nuanced, and in the process it would allow prices to more accurately reflect what consumers really value. "At the moment,



prices are good at transmitting the value of goods in strict economic terms," Parikh says. "But they're not so good at transmitting other kinds of information, like what the production of a good has taken away from the environment, or the experience of the workers producing that good. One of the things technologies allow us to do is actually convey more of that information."

It would be a mistake to see Cam and technologies like it as a panacea for the problem of underdevelopment. While it's easy to become infatuated with the promise of microfinance and small-scale entrepreneurship, it's also easy to overestimate how much influence these things can exert on developing economies, which often face structural problems that won't be solved by making local markets more efficient. And it's also the case that, in the short run at least, the arrival of new technologies can widen the gap between the prosperous and the struggling: if you're buying more from the Cam-equipped farmers, you'll probably buy less from the non-Cam-equipped ones. In other words, not everyone will win.

Parikh seems well aware of the limits of technology in general and Cam in particular. But he is also convinced that mobile phones have the capability to become far more powerful tools, which is why he has other applications in mind for Cam-such as tracking disease outbreaks and improving the coördination of relief after disasters. In each case, one can observe Parikh's respect for the virtues of decentralized organization and the conviction that bringing more information and more transparency to social systems is better. Parikh is focused more on solving real problems than on developing complex technologies. "I think oftentimes with formal and well-established disciplines like computer science, you run into the problem of inertia, a kind of hesitancy to accept new ideas about what should count as important," he says. "But I'm cautiously optimistic that within academia as a whole, there's a broad sense that the realworld impact of someone's work is an important criterion by which to judge it. Ultimately, I think that's what counts: how can the work we do have a practical impact? How can it make a difference in the way people live?"





Florida:

PANEL #1

CHANGE Y

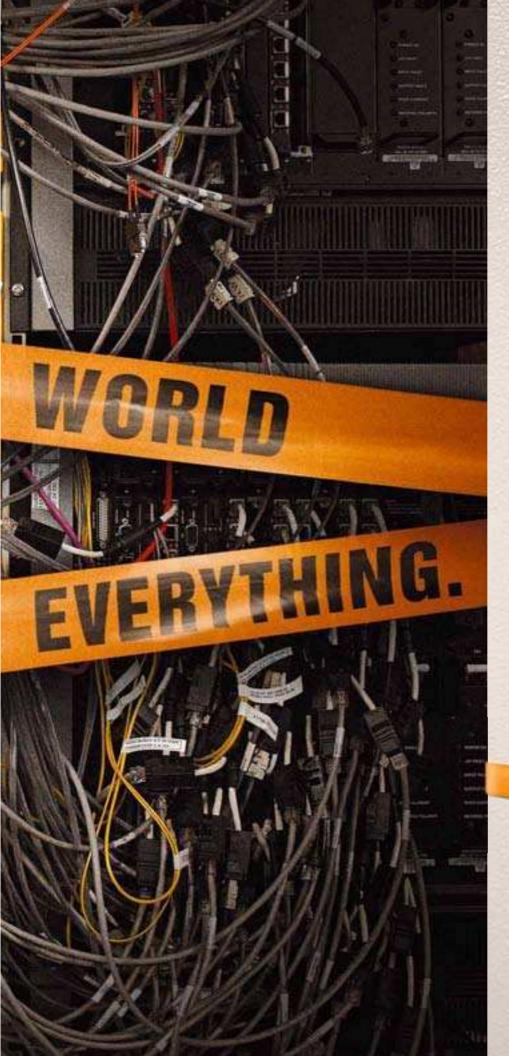
SHELF #4

WITHOUT CHANGING

SHELF#3



SHELF #2



Don't touch it. Don't move it.

Contrary to what they might say,
VoIP isn't synonymous with "starting
over." It isn't about ripping and replacing
or big, upfront costs. That's because it's
no longer about hardware.

It's actually about software.

Now you can keep your hardware—your PBX, your gateways, even your phones. Simply move to VoIP with software. Software that integrates with Active Directory, Microsoft Office, Microsoft Exchange Server, and your PBX.

Maximize your current PBX investment and make it part of your new software-based VoIP solution from Microsoft. You're much closer to VoIP than you realize. Learn more at microsoft.com/voip

VOIP AS YOU ARE.

Your potential. Our passion.*

Microsoft*





SOFTWARE

Desney Tan, 31

Teaching computers to read minds

Tan's Microsoft Research office and find him wearing a red and blue electroencephalography (EEG) cap, white wires cascading past his shoulders. Tan spends his days looking at a monitor, inspecting and modifying the mess of squiggles that approximate his brain's electrical activity. He is using algorithms to sort through and make sense of EEG data in hopes of turning electrodes into meaningful input devices for computers, as common as the mouse and keyboard.

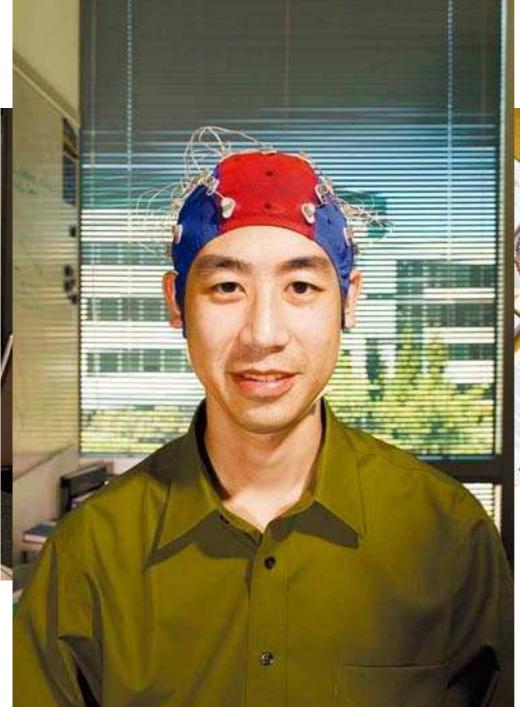
The payoff, he says, will be technology that improves productivity in the

workplace, enhances video-game play, and simplifies interactions with computers. Ultimately, Tan hopes to develop a mass-market EEG system consisting of a small number of electrodes that, affixed to a person's head, communicate wirelessly with software on a PC. The software could keep e-mail at bay if the user is concentrating, or select background music to suit different moods.

As early as 1929, researchers observed slight changes in EEG output that corresponded to mental exertion. But these results haven't led to a massmarket computer-input device, for a number of reasons. Most EEG exper-

iments are conducted in labs where electrical "noise" has been minimized, but outside the lab, EEG is susceptible to electrical interference. EEG equipment also tends to be expensive. And previous research has averaged data from many users over long periods of time; some studies have shown that individual results vary widely.

Tan believes he can solve these problems by training machine-learning algorithms—often used to understand speech and recognize photos—to account for variations between individuals' EEG patterns and to distinguish interesting electrical signals from junk. Contrary to popular practice, Tan keeps his lab as electrically noisy as the average home or office. He is even using the least expensive EEG equipment he could find—a kit he bought for a couple of hundred dollars at a New Age store. (Some people use EEG for meditation.)





(center) wears an electroencephalography (EEG) cap, a device that measures electrical potentials created by brain activity. At left, Tan analyzes a subject's EEG readings as part of a project to create software that can gauge a user's concentration level. At right, brain diagrams, research papers, and extra EEG leads decorate a bulletin board in Tan's office.

Tan's EEG cap has 32 electrodes that are affixed to the scalp with a conductive gel or paste. When neurons fire, they produce an electrical signal of a few millivolts. Electronics within the device record the voltage at each electrode, relative to the others, and send that data to a computer.

A subject using Tan's system spends 10 to 20 minutes performing a series of tasks that require either high or low concentration-such as remembering letters or images for various amounts of time. EEG readings taken during the activity are fed to a computer, which manipulates them mathematically to generate thousands of derivations called "features." The machine-learning algorithm then sifts through the features, identifying patterns that reliably indicate the subject's concentration level when the data was collected. Tan and his collaborators at the University of Washington, Seattle, and Carnegie Mellon University have shown that a winnowed set of about 30 features can predict a subject's concentration level with 99 percent accuracy.

Tan expects the technology to be used initially as a controller for video games, since gamers are accustomed to "strapping on new devices," he says. In fact, next year a company called Emotiv Systems, based in San Francisco, plans to offer an EEG product that controls certain aspects of video games. However, the company will not discuss the specifics of its technology, and there isn't widespread consensus on the feasibility and accuracy of the approach.

The true challenge, Tan says, will be to make EEG interfaces simple enough for the masses. He and his team are working on minimizing the number of electrodes, finding a semisolid material as an alternative to the conductive gel, and developing wireless electrodes. A mass-market product could be many years away. But if Tan succeeds, getting a computer to read your thoughts could be as easy as putting on a Bluetooth headset. -Kate Greene



HARDWARE

Babak Parviz, 34

University of Washington

Self-assembling micromachines

PROBLEM: Relatively simple microelectromechanical systems are already used in air bags and other devices, but MEMS of greater complexity hold promise in applications ranging from medical implants to advanced navigation devices. Such machines might include components like tiny sensors, motors, and power sources. The methods for manufacturing these diverse parts, however, are largely incompatible, which makes assembling complex MEMS on a large scale and at a reasonable cost impossible.

SOLUTION: Babak Parviz, an assistant professor of electrical engineering, has developed a method of coaxing individual components to



assemble themselves into MEMS devices. Recently, he used it to build a working singlecrystal silicon circuit on a flexible plastic substrate; the two materials

are difficult to combine using conventional manufacturing methods.

Parviz began by manufacturing micrometer-size silicon parts in bulk. He also designed a plastic substrate with binding sites whose shapes complemented those of the silicon components. Parviz immersed the substrate in a fluid containing the silicon parts, which quickly attached to their binding sites. Metal interconnects embedded in the plastic completed the circuitry.

Such silicon-on-plastic devices could form the basis for flexible displays, biosensors, and low-cost solar panels. Parviz says that self-assembly offers the ability to efficiently and cheaply manufacture multifunctional devices of all sizes from nanoscale components. —Corinna Wu

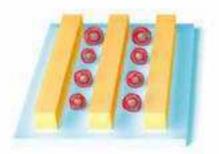
MEDICINE

Ali Khademhosseini, 31

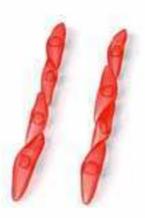
Harvard-MIT Division of Health Sciences and Technology Living Legos

The ability to create living tissues and organs in the lab holds great promise for transplant medicine. But the traditional approach to tissue engineering—seeding the outside of a biodegradable scaffold with cells, without regard to their organization—hasn't gotten cells to behave the way they would in the body.

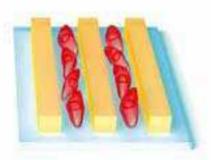
Ali Khademhosseini, assistant professor in medicine and health sciences and technology at Harvard Medical School, hopes to improve engineered tissues with an approach he likens to building with living Legos. As a first step toward creating a heart, he aligns cardiac muscle cells to form small, beating strings. He then embeds these strings in a supportive, gelatinous polymer to make building blocks that can be assembled into bundles resembling the sheets of muscle that make up the heart. He can also add other types of cells to the building blocks to provide support for the muscle. This aspect of the system is crucial, since natural tissues comprise cells of multiple types in structurally complex arrangements. By giving cells the same interconnections they have in the body, Khademhosseini hopes to create tissues that can be used to test new drugs and, eventually, to rebuild organs. —Katherine Bourzac



 Khademhosseini begins by seeding a patterned slide with heart muscle cells



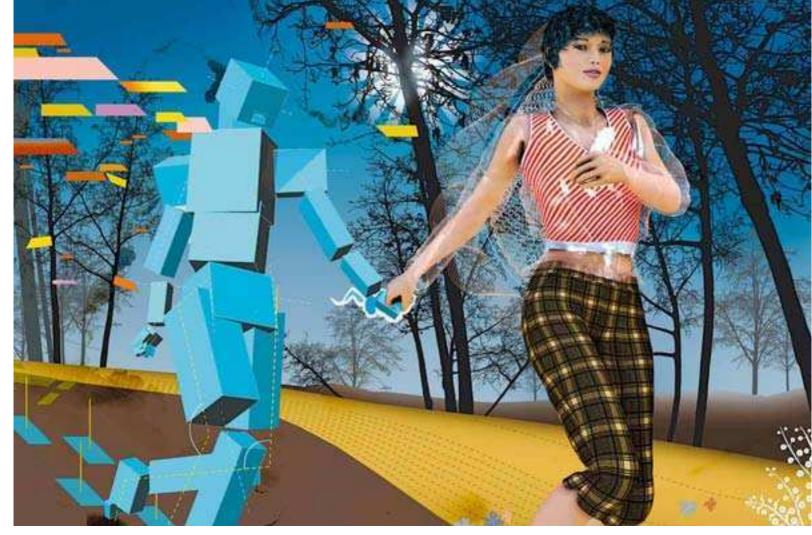
After six days, the cells have formed "organoids" that beat on their own and may be removed from the slide



2) Guided by the pattern, the cells elongate until they resemble the cells in a living heart



 The organoids are embedded into blocks of gel that can be molded into any shape needed—and combined like tissue-engineering "Legos"



Karen Liu, 30

Bringing body language to computer-animated characters

crowded sidewalk is a cacophony of unspoken yet unmistakable Lmessages. A young woman's "I feel sexy" walk, for instance, is instantly distinguishable from a biker dude's "Don't mess with me" stride. But getting computer-generated (CG) characters to reproduce physical attitudes like these is still an arcane craft. Animators must either eveball characters' movements in hundreds of hand-drawn "key frames," with software interpolating the in-between moments, or cheat by using expensive motion-capture systems to digitize the behavior of real actors.

As a computer science graduate student at the University of Washington in the early 2000s, Karen Liu set out to find an easier method. Her article

of faith: "There [had] to be some way, from our knowledge of physics and biomechanics, to distill the properties that create motion styles."

Biomechanics researchers had long been analyzing the mechanical factors that affect the way people move. Simulating those factors, Liu thought, would yield CG characters that move more naturally. But the human body contains hundreds of interacting parts, and it was impractical to measure or even stipulate the values of parameters such as tension and elasticity for every muscle, tendon, and ligament. Working with advisor Zoran Popović, Liu eventually showed that feeding just a handful of these values into animation software is enough to reproduce a distinctive motion such as a "happy walk" in a range of CG models, from people to penguins.

To establish her style parameters, Liu developed algorithms based on a single, simplifying assumption: that people naturally try to waste as little energy as possible when they move. Into these algorithms she feeds short segments of motion-capture data from subjects instructed to move in a certain way—to walk happily, for example. The software then reasons backward to guess the values of certain parameters, choosing those values that would have made the movements energy efficient.

Liu, who just joined the computer science faculty at Georgia Tech, is talking with major game makers and film studios about applying her algorithms to video games and animated films. She hopes the algorithms will help animators create CG humans that move more naturally than the robotically stiff characters in films like The Polar Express. "I think we're really close," she says. -Wade Roush

Christopher Loose, 27

SteriCoat
Beating up bacteria

PROBLEM: Each year, a million Americans suffer infections related to medical devices such as the intravenous lines that deliver chemotherapy and liquid nutrition. Adding slow-release antibiotic coatings to the devices helps prevent such infections, but the coatings become inactive when all the drugs have been released, and bacteria can become resistant to them.

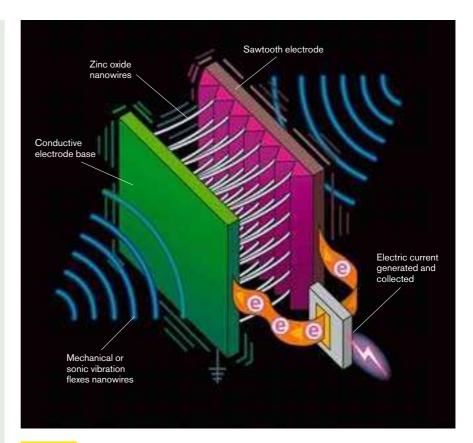
SOLUTION: As a graduate student at MIT, Christopher Loose created a design tool to optimize formulations of naturally occurring antibiotics called antimicrobial peptides (AMPs),



and developed a way to use them in medical devices. Found in bacteria, human sweat, and plants, these short proteins puncture bacteria like balloons. The mech-

anism is nonspecific, so microbes have trouble developing resistance to the peptides.

But AMPs are too expensive for routine oral or intravenous use. So Loose incorporated optimized peptides into coatings for medical devices, which are effective with a small amount of peptide. When bacteria approach a hip implant or catheter coated with the peptides, they "see a bed of nails," says Loose. The coating doesn't release the drugs the way typical antibacterial coatings do, so its activity is potentially permanent, Loose founded SteriCoat to commercialize the technology and is currently its chief technology officer; the company is testing coated intravenous lines in animals and hopes to bring them to market in 2011. -Katherine Bourzac



ENERGY

Xudong Wang, 31

Powering the nanoworld

his PhD in materials science at Georgia Tech at the end of 2005, he knew he had a good thing going. He opted to stay put in the lab of Zhong Lin Wang (no relation), sure that he and his lab mates were close to creating a new nanotech-based generator—an invention they felt could change the future of nanotechnology.

His risk paid off earlier this year when *Science* published a paper he coauthored, describing a novel device that converts ultrasonic waves—high-frequency mechanical vibrations—into electricity. The tiny device turns out a steady 0.5 nanoamperes of current that engineers may one day be able use to power implantable biosensors, remote environmental monitors, and more.

"It's a very cool concept," says Peidong Yang, a nanowire researcher at the University of California, Berkeley. "Vibrational energy is everywhere." If Wang's devices can harness it cheaply, "the impact could be big," Yang says.

The generator is the culmination of several remarkable advances made by Wang since he arrived in Z. L. Wang's lab from China in 2002. Others had made nanowires of zinc oxide (ZnO), a versatile optical, semiconductor, and piezoelectric material, but the production process typically left them tangled like spaghetti. Many prospective uses of nanowires, however, require that they form an orderly array. By 2004, Xudong had found a way to use gold to catalyze the emergence of an organized forest of wires from a vapor of zinc oxide dust.



While Xudong was finishing up his PhD, Z. L. Wang and Jinhui Song, another graduate student in the lab, showed that they could generate a tiny electric current by bending individual ZnO nanowires with the tip of an atomic force microscope. Still, to make practical energy harvesters, the researchers needed a way to collect energy from thousands of nanowires flexing simultaneously.

They began with one of Xudong Wang's miniature ZnO forests, grown atop an electrode made from gallium nitride, sapphire, or a conducting polymer. Xudong capped this with a second electrode made of platinum-coated silicon and studded with parallel rows of tiny peaks and trenches, like lines of saw teeth. He then used ultrasound waves to vibrate the electrodes. The motion squeezed the two electrodes together, causing the nanowires between them to flex and generate a current; the current flowed through the platinum coating and into an external circuit.

Conceiving the generator was a group effort, but Z. L. Wang gives Xudong credit for pulling off the demonstration. "Anything you can think up, he can make it work," Z. L. says.

The two-square-millimeter devices turn out just a trickle of power, but in the months since its *Science* paper appeared, the team has already boosted the devices' output current 30-fold. And there's plenty of room for improvement: ensuring that all the nanowires are actively generating current, for example, could boost the power output to as much as four watts per cubic centimeter. "If we do that, we can power portable electronics such as cell phones," Xudong says. The group is also trying to make versions of the device that generate current in response to lower-frequency sound waves and to mechanical vibrations. That could allow nanotechnologists to harvest energy anywhere, from the interior of a pulsing blood vessel to the chassis of a car rattling down the highway. -Robert F. Service

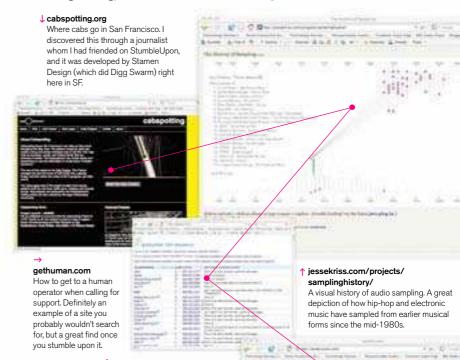
INTERNET

Garrett Camp, 28

StumbleUpon
Discovering more
of the Web

In 2001, Garrett Camp and two friends began working—"out of our bedrooms," he says—on a tool to help people serendipitously discover interesting Web content. Camp, who was then a grad student in software engineering, has guided the research behind the site and the design of its architecture ever since. In May, eBay acquired the Web 2.0 "discovery engine" for approximately \$75 million. As of July, more than three million users had downloaded the StumbleUpon toolbar; the simple interface consists of a row of about 15 buttons at the top of a Web browser. Clicking "I like it" when viewing a site amounts to a recommendation; clicking

the thumbs-down button submits a negative review. Clicking "Stumble" takes a user to one of more than 10 million sites recommended by friends or other users with similar interests. The system refines individual recommendations on the basis of the user's previous reviews and the preferences of users whom the site judges to have similar tastes. So what kinds of sites has Camp stumbled upon? Take a sneak peek here. -Erika Jonietz



TRIBLEZEN, ZIRRERE

twittervision.com

Twittervision is a mashup between

the text-message blogging service

Twitter and Google Maps. It shows you what people across the globe

are blogging from their phones at

A visual exploration of computation using Flash. StumbleUpon is great for discovering graphical content such as art, photos, and videos, and this is a perfect example of a graphics-rich site that doesn't contain a lot of keywords you might search for yet is an interesting discovery when you're stumbling through graphics or design sites.

levitated.net/exhibit/

index.html





TELECOM

Mung Chiang, 30 Princeton University Optimizing networks

Mung Chiang likes to say that there's nothing more practical than a good theory. An assistant professor of electrical engineering, he improves the design of telecommunications networks by applying the mathematics of optimization theory. Through industry collaborations, his algorithms are revolutionizing the backbone of the Internet, the broadband connections that bring data and video to homes and offices, and wireless networks of every stripe.

In one project, Chiang and coworkers found a way around the limits of the current Internet routing protocol, which sends packets along the shortest available paths on the network. It's a seemingly straightforward strategy that ends up causing complex network-management problems. The researchers realized there were advantages to sending the occasional packet along a longer path; the new algorithm achieves the lowest computational cost possible for a routing protocol and increases network capacity by 15 percent—without adding equipment to the network.



SOFTWARE

Josh Bongard, 33

Adaptive robots

Josh Bongard's robot walks with a limp. But it's impressive that it walks at all.

As a postdoc at Cornell, Bongard collaborated with roboticist Hod Lipson and PhD student Victor Zykov to develop a robot that can adapt to changes in its body or in the environment—a key advance for robots designed to work outside a controlled laboratory setting. Bongard, now an assistant professor of computer science, begins by programming his robot with basic information about its design, such as the mass and shape of each of its parts. In his standard demonstration, he then disconnects one of its four legs. To get a

sense of its handicap, the robot rocks back and forth, activating two tilt sensors. It then builds a virtual model of itself, using simulation software, and uses that model to test new ways of walking despite its handicap. Once the robot has developed a successful simulation, it attempts to walk using the same technique.

Rodney Brooks, professor of robotics at MIT, says that Bongard's work is interesting because it's inspired by the way biological systems adapt. To meet roboticists' future goals of creating self-configuring robots, Brooks says, "these sorts of ideas are going to be essential." —Rachel Ross



Though the real-world impact of his work matters to Chiang, he says another important motivation is the beauty of an airtight mathematical proof. "I'm an engineer at heart," he says, "but a mathematician in my brain." —Brendan Borrell



BIOTECHNOLOGY

Neil Renninger, 33

Amyris Biotechnologies Hacking microbes for energy

As a former member of the infamous MIT blackjack team, Neil Renninger knows what it means to make big, calculated risks and see them pay off. Three years ago, he took just such a risk, cofounding synthetic-biology startup Amyris while a postdoc at the University of California, Berkeley. The company's new approach to biofuels is now generating serious buzz among investors and interest from corporations such as Virgin, which recently opened a fuel division.

Amyris started by commercializing a microbial approach to producing a precursor of artemisinin, a potent malaria drug (see "10 Emerging Technologies: Bacterial Factories," May 2005). Artemisinin is currently derived from sweet worm-

wood, but Renninger outlined a way that it could be made more cheaply in bacteria—helping land a share of a \$42 million grant from the Gates Foundation. He is also playing a key role in Amyris's biofuels venture. He began by identifying molecules that would work well as fuels and were compatible with existing engines and delivery infrastructures; then he found a way to combine biological and chemical processes to manufacture them. So far, Amyris has created microbes that can produce candidate replacements for biodiesel, jet fuel, and gasoline. "Now we need to tinker with the bug to squeeze out the last bit of metabolic flux that turns something from interesting to cheap enough to burn," he says. —Emily Singer



NANOTECHNOLOGY

Mehmet Yanik, 29

MIT Stopping light on microchips

Mehmet Yanik, an assistant professor of electrical engineering and computer science, has invented a way to stop light pulses on a chip and release them at will. The technology could allow engineers to route and store optical data in telecommunications networks and on microchips without having to convert it to electricity.

Yanik's system traps a pulse of light in an arrangement of microscopic cavities. A fundamental challenge in designing the system was that the faster light can enter the cavities, the faster it escapes, severely limiting how long it can be stored. To overcome this problem, Yanik developed a way to adjust the cavities' refractive index, a property related to the way a material bends or reflects light. At first, light easily slips into a cavity. Once the light is inside, a small change to the index traps it. Changing the index yet again releases it. The system works quickly, making it ideal for processing data. -Kevin Bullis

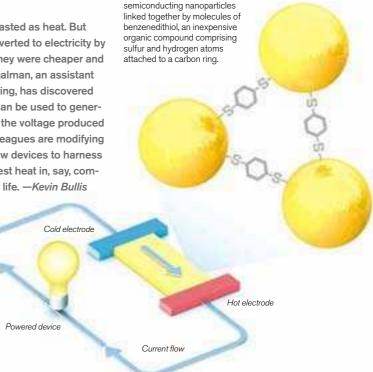
ENERGY

Rachel Segalman, 31

University of California, Berkeley Cheap electricity from heat

Most of the energy in fuels is wasted as heat. But much of that heat could be converted to electricity by "thermoelectric" materials—if they were cheaper and more efficient. Now Rachel Segalman, an assistant professor of chemical engineering, has discovered that cheap organic molecules can be used to generate electricity from heat. So far, the voltage produced is small, but Segalman and colleagues are modifying the molecules and inventing new devices to harness them. Such devices could harvest heat in, say, computers, to extend laptop battery life. —Kevin Bullis

A material combining nanoparticles and organic molecules conducts electricity but not heat—a vital property of thermoelectric materials, since it is the heat differential that creates the electrical voltage. In a thermoelectric device, the material is sandwiched between two electrodes. As one electrode is heated and the other kept cool, a voltage is produced. Hooking the electrodes to an external circuit generates a current.



Segalman's thermoelectric

material consists of metallic or

REVAN CHEISTIF

TELECOM

Marc Sciamanna, 29

École Supérieure d'Électricité and Centre National de la Recherche Scientifique (France)

Controlling chaos in telecom lasers

PROBLEM: Vertical-cavity surface-emitting lasers, or VCSELs, are commonly used in telecommunications networks, but they behave in ways scientists don't completely understand. Specifically, the polarization of the light they emit—the orientation of its magnetic field—fluctuates unpredictably. Moreover, a little optical feedback, such as light reflected from network equipment, may result in chaotic changes in the power or wavelength of the light emitted by the lasers. Engineers would like to harness all of these fluctuations to

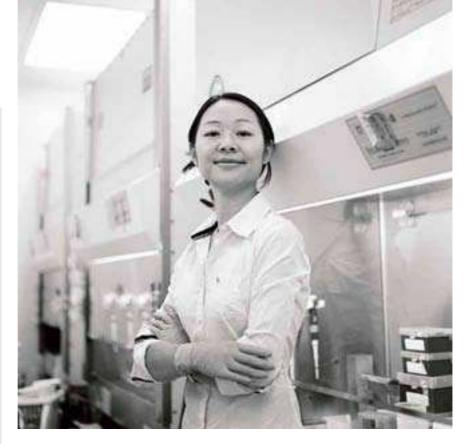


SOLUTION:

Marc Sciamanna, a professor at the École Supérieure d'Électricité in Paris, has devel-

oped a theoretical explanation of the lasers' chaotic behavior. He has also suggested different techniques for controlling VCSEL polarization and chaotic laser dynamics in general; in particular, he demonstrated that optical feedback can be used to regularize polarization. More recently, he showed that increasing the amount of noise, or random fluctuation, in the electrical current that powers the lasers would make the variations in polarization more predictable and also stabilize the chaotic output. If light polarization and chaotic dynamics were subject to engineers' control, they could be used to encode digital information-significantly expanding Internet bandwidth.

-Kate Greene



BIOTECHNOLOGY

Lili Yang, 32

Engineering immunity

he immune system is a sophisticated machine, designed to fend off a constant barrage of disease-causing microbes. Unfortunately, it's not as good at fighting cancer, which disguises itself as normal tissue. Using gene therapy, Lili Yang is reprogramming the immune system to recognize and kill cancer cells.

Stimulating the immune system to fight cancer is one of today's hottest research areas. Some scientists hope to genetically modify patients' white blood cells to do the job, but Yang is altering the body's blood-forming stem cells, a technique that could prove much more powerful. Because stem cells are self-renewing, they could generate a lifelong supply of immune cells programmed to combat, or even prevent, the disease.

A project manager and lead scientist in Caltech's Engineering Immunity Program, Yang created a viral "vector" that simultaneously delivers two genes to the stem cells: the genes encode the T-cell receptor protein, which enables white blood cells called T cells to recognize and kill cancer cells. The modified stem cells then give rise to T cells that bear the receptor. The technique has so successfully suppressed tumors in mice that Yang plans to begin trials this spring in melanoma patients.

In order to treat patients, Yang will have to isolate and modify their blood-forming stem cells in the lab and then reinject them—a laborious, costly process. So she is collaborating with her husband, Pin Wang of the University of Southern California, to design viral vectors that can deliver therapeutic genes to only one cell type. They have succeeded in mice, a significant advance in gene therapy.

In the future, says Yang, treating cancer could be as simple as injecting patients with such targeted vectors. Gene therapy has yet to live up to its huge potential, but "Lili has the ability to make it a part of modern medicine," says Caltech biologist and Nobel Prize winner David Baltimore, Yang's supervisor. Indeed, Yang is also creating vectors to stimulate specific immune cells to make antibodies against HIV. If successful, that project could at last lead to an AIDS vaccine. —Alexandra Goho

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The Enthusiast

A controversial Harvard biologist says he's found a way to extend life span and treat diseases of aging. He's shown that it works in mice. Will it also work in humans?

By David Ewing Duncan

Portrait by Steve Brodner

avid Sinclair is very good at persuading people. The catch, says a longtime colleague and scientific rival, is that he is sometimes overly optimistic about his results. "David is brilliant, but sometimes he is too passionate and impatient for a scientist," says another colleague. "So far, he is fortunate that his claims have turned out to be mostly true."

Sinclair's basic claim is simple, if seemingly improbable: he has found an elixir of youth. In his Australian drawl, the 58-year-old Harvard University professor of pathology explains how he discovered that resveratrol, a chemical found in red wine, extends life span in mice by up to 24 percent and in other animals, including flies and worms, by as much as 59 percent. Sinclair hopes that resveratrol will bump up the life span of people, too. "The system at work in the mice and other organisms is evolutionarily very old, so I suspect that what works in mice will work in humans," he says.

Sinclair thinks resveratrol works by activating *SIRT1*, a gene that many scientists believe plays a fundamental role in regulating life span in animals. Biologists have found that increasing the expression of *SIRT1* slows aging and fends off maladies associated with growing old, including cancer and heart disease. If Sinclair is right, and resveratrol can activate *SIRT1*—and if the gene does in fact help control aging—he has found something truly remarkable.

The scientific uncertainty surrounding Sinclair's claims hasn't stopped him from raising millions of dollars. In 2004 it took him a single lunch meeting to persuade California philanthropist Paul Glenn to put up \$5 million for a new Harvard institute on aging, of which Sinclair is now a director. Sinclair also cofounded Sirtris Pharmaceuticals to develop drugs based on resveratrol and helped persuade an A-list of venture investors to pony up \$103 million in private funding. In late May, the company made an initial pub-

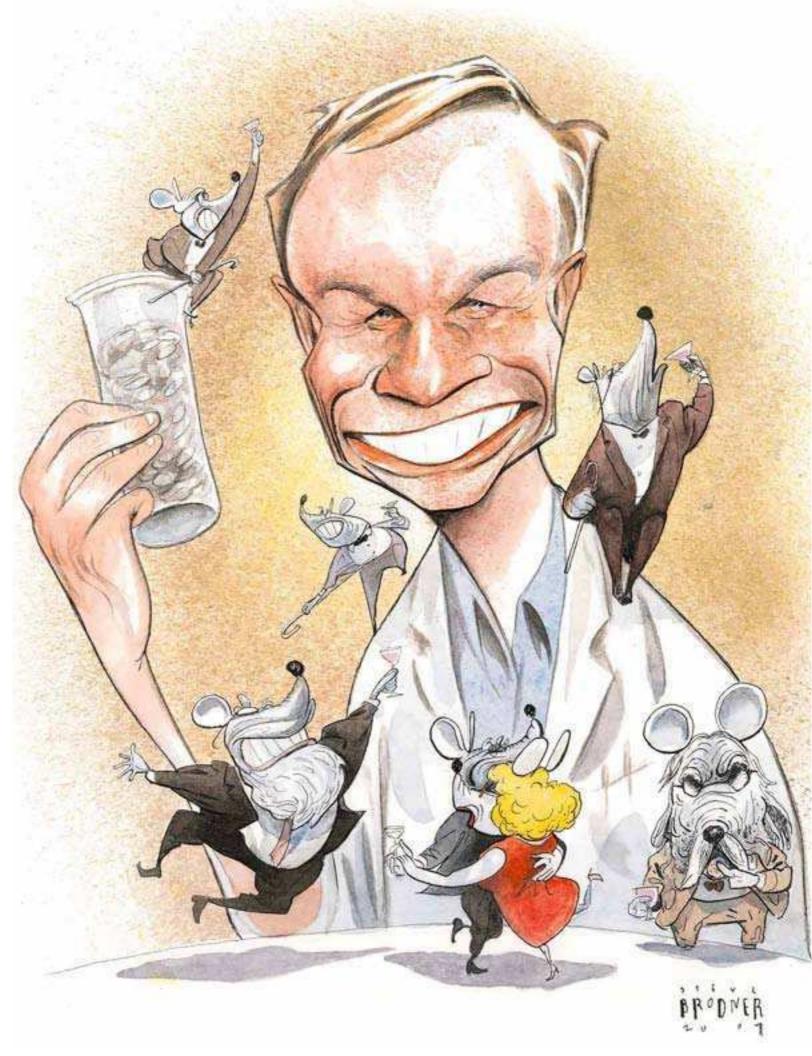
lic offering that netted \$62 million more. The stock price quickly rose 20 percent, providing Sinclair, who holds less than 1 percent of the shares, with a pleasant (if, for now, notional) addition to his academic salary—and possibly a big payday should the company ever produce a fountain-of-youth pill. "I grew up middle class in Sydney," he says, flashing a characteristically shy though confident smile. "As an academic, I never expected to be wealthy, so any extra is unexpected, although [it] feels pretty good."

Later, Sinclair winces when I mention that some colleagues describe him as a good salesman. "Scientists don't like to be called salesmen," he says. "It's an insult." Still, he says, "I believe in my work and advocate for my conclusions." One thing is certain: Sinclair's persuasiveness gives him an edge over his rivals in a field where a good deal of money and glory is at stake—not to mention potential impact on the future of medicine.

Obsessed

Sinclair says his bravado and drive come from his grand-mother Vera, who fled to Australia in the wake of the failed 1956 revolution in her native Hungary. Her son, David's father, changed the family name from Szigeti. "My grand-mother is the black-sheep rebel of the family," he says. "She gave birth to my dad at age 15 in 1939—imagine the scandal then—and has lived with natives in New Guinea and eaten human flesh, among other things. She once got in trouble with the police for being the first person to wear a bikini on a Sydney beach. She's a '60s bohemian who helped raise me and taught me how to think differently and to question dogma."

A slight man with a mischievous smile, Sinclair grew up in St. Ives, near Sydney, where as a boy he liked to make bombs from chlorine or gunpowder to blow things up. "It was rebel-



lious and dangerous," he says. "That was the thrill. I think I was bored." When he was seven years old, he came up with a list of 10 ways to change the world, and one was to create inventions to make money. Later, he took up windsurfing and racing around in cars. He got so many speeding tickets that he once had his license confiscated. "He was always quite cheeky and could get under your skin if he knew you well enough," says Mark Sumich, his best friend growing up.

"I think the day I got most scared in my life was when he showed me his brother's new compound bow," recalls Sumich, who now owns a market-research company in Australia. "We went up to the park, and he would shoot it straight up in the air, and having lost sight of it, we would scatter for cover. That, to this day, is still the most stupid thing I have ever done."

Sinclair attended the University of New South Wales and was studying gene regulation in yeast when he learned about longevity research during a conversation with Leonard Guarente, an MIT molecular biologist who was in Australia giving lectures. Back then—1993—most people assumed that aging was a complex and inevitable process that could not be regulated by just a few genes. But that year, Cynthia Kenyon, a biologist at the University of California, San Francisco, published a study showing how manipulating a single gene, *daf2*, could double the life span of a tiny roundworm. Guarente himself was beginning experiments on yeast that would lead to the discovery of the antiaging gene *sir2* in 1995.

The field was so new and unproven, though, that Guarente talked about it only informally—as, for instance, when a young Australian scientist sat down next to him during a group lunch. "This was incredibly serendipitous," says Sinclair. Inspired, he sold his Mazda Miata to buy a ticket to Boston to interview for a postdoc position in Guarente's lab. During his interview, he gave a spirited whiteboard presentation arguing that scientists studying aging should look for genes that prolong life rather than genes and mechanisms that end it. He got the job.

While Sinclair was in Guarente's lab in the late 1990s, he discovered that *sir2* prevents aging in yeast by slowing down the accumulation of ERCs, circular strands of DNA that build up in organisms as they age, eventually killing them. Around the same time, others in Guarente's lab made another crucial discovery: that a link may exist between *sir2* and a molecule critical for metabolizing food, called NAD. The connection suggested that the longevity gene might be related to diet—specifically, Guarente postulated, to caloric restriction. A nutritionally complete diet containing 30 to 40 percent fewer calories than normal had long been known to extend life span in some animals, ramping up cell defenses and slowing down aging. Guarente and others theorize that in times of scarcity, such as famine or drought, this mechanism allows an organism to survive—

and postpone reproduction—until the crisis is over. The link between *sir2* and NAD, therefore, suggested to Guarente that caloric restriction might be affecting longevity by activating the antiaging gene.

Colleagues who were students in Guarente's lab during this period remember Sinclair as highly ambitious. Shin-ichiro Imai, then a postdoc, now a molecular biologist at Washington University in St. Louis, and still a friend, describes him as "obsessed," with a penchant for aggressively pursuing his ideas. "He is an introvert who becomes an extrovert for what he's working on," Imai says.

Sinclair's ambition has also complicated his relationship with his mentor, who helped him secure an appointment in Harvard Medical School's department of pathology in 1999. Guarente, a lanky man with a shaved head and intense eyes, says he is proud of his protégé. In 2004, however, an article in *Science* described a rivalry between the two men that began during a meeting at Cold Spring Harbor in New York, where Sinclair stunned Guarente by disagreeing with him about how a key gene associated with caloric restriction increases life span in yeast. The two began publishing competing papers, vying head to head to figure out how *sir2* and, later, other antiaging genes are regulated. "Most young scientists would not compete directly with their mentors, but David did," says Imai.

Sinclair also said no to signing on with Elixir Pharmaceuticals, the company cofounded by Guarente and Cynthia Kenyon in 1999, which for a time he had hoped to join. By the time Elixir called, he had discovered the effects of resveratrol; in 2004 he surprised his former teacher by cofounding Sirtris, a company whose name incorporated that of the *SIR* genes that Guarente had helped to discover.

Both men say that *Science* overstated the extent of the rift between them. There was some tension for a couple of years, they say, but that has died down. They now collaborate on some experiments and articles, and they talk frequently. In a curious turnaround, Guarente left Elixir last year and has considered working with Sirtris, although he can't join the company until the fall of 2007 because of a one-year noncompete clause in his contract with Elixir.

Breakthrough

In 2005, one unsolved mystery among the still-small cadre of longevity researchers was how to modulate genes, such as *SIRT1*, that regulate life span. Was there a compound that could be taken as a pill? Elixir and other companies and labs were beginning to screen thousands of chemicals to see if one would work as a gene activator, but none fit the bill.

To read a detailed explanation of the science behind resveratrol and sirtuins, go to **technologyreview.com/sirtuins**.

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In February 2005, in what was then his small, shoestring lab at Harvard, Sinclair was doing his own screening when he learned that scientists at Biomol Research Laboratories, a biotech company in Plymouth Meeting, PA, had observed that *SIRT1* was activated by certain polyphenols, including resveratrol. Sinclair and Konrad Howitz, Biomol's director of molecular biology, collaborated to isolate resveratrol and test it in yeast and fruit flies. "Never in my wildest dreams did I think we would find an activator of *sir2*," says Sinclair.

In a 2004 *Science* interview, Sinclair added to his reputation as a zealot, calling resveratrol "as close to a miraculous molecule as you can find." "One hundred years from now," he said, "people will maybe be taking these molecules on a daily basis to prevent heart disease, stroke, and cancer."

That same year, two scientists who were students in Guarente's lab when Sinclair was there published a paper casting doubt on the underpinning of Guarente's hypothesis that caloric restriction activates sir2—a hypothesis that is critical to Sinclair's own theories. ("I have independent-minded students, I guess," Guarente told me with a wry smile.) The former students, Brian Kennedy and Matt Kaeberlein,

both biologists at the University of Washington, claimed that, at least in yeast, caloric restriction could exert antiaging effects in the absence of sirtuins—the enzymes produced by *sir2* and its mammalian homologues (such as *SIRT1*). Studies published soon after posed a more direct challenge to Sinclair's contention that resveratrol mimics caloric restriction by activating sirtuins. Peter

DiStefano, a coauthor of one of these studies and the chief scientific officer of Elixir, told me in 2005 that resveratrol does wondrous things, but it is unlikely to be an activator of the SIRT1 enzyme.

That skepticism, however, didn't deter Sinclair. In 2004 he set out to prove that resveratrol indeed mimicked some effects of caloric restriction, joining with Rafael de Cabo of the National Institute on Aging to test the chemical on mice.

Mice live about two to three years; when I first visited Sinclair's lab, in 2005, his test mice were about a year old. Sinclair was already ecstatic, because the resveratrol-fed mice seemed healthier than the controls; their cells were also aging remarkably slowly, even though the mice were being fed a fatty, unhealthy diet. When the paper on these experiments came out the following year in *Nature*, the results supported the claims Sinclair had been making about resveratrol in mammals. They showed that mice on a high-fat diet fed large doses of resveratrol were as healthy as mice on a regular diet. Resveratrol also improved the mice's insulin sensitivity and increased their energy production.

The mice were given very high doses of resveratrol—22 milligrams per kilogram of weight. In comparison, a

liter of red wine delivers 1.5 to 3 milligrams. To consume resveratrol at the same rate as the mice, a 150-pound human would need to drink roughly 1,500 bottles of wine (or take scores of pills) each day.

Sinclair's paper came out within days of a study in *Cell* from the lab of Johan Auwerx of the Institute of Genetics and Molecular and Cellular Biology in Illkirch, France. Auwerx's team, which was partially funded by Sirtris (Auwerx is on the company's scientific advisory board), had given mice even higher doses of resveratrol—400 milligrams per kilogram. These mice stayed slender and strong on a high-fat diet, with the energy-charged muscles and reduced heart rate of athletes. The number of mitochondria in their cells increased, which improved the cells' energy output.

Sinclair's and Auwerx's success in extending the life span and improving the health of mice has partly assuaged critics' doubts that resveratrol can work in mammals. "Both studies are extremely exciting," says Kaeberlein; it's "pretty clear" that resveratrol modifies certain proteins, such as mitochondrial proteins associated with energy production.

"This will impact humans within a decade. That's why I don't think there is anything more important than this quest. That's why I take chances, and why the controversy is worth it: because I think we are right."

> Kaeberlein points out, however, that the tests involved mice on a high-fat diet and should be duplicated with mice on a normal diet.

> And Kaeberlein is not yet convinced that resveratrol is an activator of the SIRT1 enzyme. "We were unable to reproduce the work from the Sinclair lab in yeast," he says, adding that results have been mixed in flies, worms, and other animals. He also still disagrees that sir2 is the pathway by which caloric restriction increases longevity in yeast. "Sir2 regulates longevity, and caloric restriction regulates longevity," he says. But it doesn't follow that caloric restriction necessarily increases life span by activating sir2.

Critics point out, too, that no one yet knows whether resveratrol will work in humans. According to Harvard population biologist Lloyd Demetrius, the evolutionary forces determining life span are so radically different in mice and humans that mechanisms responsible for slower aging in mice are unlikely to have much effect in people. Demetrius has studied caloric restriction, not resveratrol, but he's still skeptical of the chemical's viability as a drug. "I think its effects on the maximal life span in humans will be almost zero," he says.

A Believer

One convert to Sinclair's views on the effects of resveratrol was Christoph Westphal, then a partner at Polaris Venture Partners, based in Waltham, MA. Though only 35 years old, Westphal had already cofounded two publicly traded companies, Momenta Pharmaceuticals and Alnylam Pharmaceuticals—both Cambridge, MA, biotech startups developing novel drugs. Westphal read the paper and e-mailed Sinclair, who was already working on starting a company. Sinclair had had someone else in mind as CEO, but he and Westphal hit it off.

"David was young and controversial," says Westphal. "Half the people thought he was crazy, and they were pounding on him. But I saw something in him and believed in his science." Westphal and Sinclair are now close friends, with adjacent desks in a small office at Sirtris. Sinclair spends his Saturdays at work, often bringing his two older children to play with Westphal's two kids. Sinclair says that he and Westphal exchange 50 e-mails a day.

I accompanied Westphal one day last winter on his morning walk from his home in Brookline, MA, across the Charles River to Sirtris's offices in Cambridge. He explained that Sirtris's intention is not to produce drugs that extend life span. "That is not an end point recognized by the FDA," he said. "Our end points will be specific diseases." The company has developed a supercharged version of resveratrol, called SRT501. It has also discovered novel small molecules that are not related to resveratrol but, it claims, are a thousand times as potent in activating the sirtuins. So far, animal tests have shown that the drugs may help treat neurological disorders and diabetes.

This past spring, the company launched phase I human trials of SRT501 in patients with diabetes; it also plans human trials later this year to test the drug as a treatment for Melas syndrome, a rare disorder that hastens aging and causes fatal deterioration of the brain and muscles. Sirtris expects to begin human trials of its non-resveratrol compounds in the first half of 2008.

Keeping Score

From his modern ninth-floor office on the Harvard Medical School Campus in Boston, Sinclair has a view that includes Fenway Park. "I can see the scores light up at night," he says. I'm there on an oddly warm day in January, when a few trees are budding and the sky is crystal blue. On a shelf are a book by the Australian golfer Greg Norman called *The Way of the Shark* and a number of textbooks. Behind Sinclair's desk are pictures of his wife and children.

Sinclair's Harvard lab, now well funded, is working feverishly to clarify the health benefits of resveratrol and other compounds, and to discover exactly how sirtuins work on aging and the diseases of aging. In experiments involving thousands of mice, researchers are homing in on different sirtuin pathways and determining how they affect different diseases. Sinclair smiles and tells me they are getting great results, but he can't say any more on the record. He does say he is working with Guarente on some experiments. "Lenny and I typically don't work on things that aren't important," he says.

It has been two years since I last saw him, and in that time Sinclair has become more seasoned, more confident about fending off critics, and more comfortable with his stance as a scientist-zealot. "I am a science rebel," he says. "That's who I am. Everything we publish is criticized."

In the conference room where I join his team to watch a presentation, the table is made of blond wood, and the black mesh chairs look expensive. Sinclair is dressed conservatively in a dark-red button-down shirt and gray slacks—not exactly the clothes of a rebel. A postdoc, Juan J. Carmona, gives a talk about what happens to the *SIR* system when a worm is exposed to the stressor of heat; Sinclair asks questions, pushing hard. Like most leading academic scientists with labs, he does little bench research himself, leaving the experiments to his students. His own success is highly dependent on their work. In the end, Sinclair looks pleased when Carmona describes how heat activated the *sir2* pathway and increased life span in the worms.

Students in Sinclair's lab say he sometimes seems driven, and he admits that he is: "I'm driven to get to goals as fast as possible. It frustrates people in my lab who have something they think is cool, but if it doesn't move us forward, I don't want to do it." He says he views all the experiments being done at Sirtris, all his work, as part of a master plan. "I see this laid out in my mind, every step. But it's happening faster than I imagined—it's taking 10 years instead of 20 years."

"When will it be ready for humans?" I ask.

"This will impact humans within a decade," he says. "That's why I don't think there is anything more important than this quest. That's why I take chances, and why the controversy is worth it: because I think we are right."

He is also not averse to discussing the possibility that a Nobel Prize will someday be awarded to longevity researchers—something Lenny Guarente has also mentioned, though with the "I don't really think much about it" attitude that is typical of senior scientists talking about the ultimate award. If such a prize is given, Sinclair says, Guarente and Cynthia Kenyon are likely to be two of the winners—out of a possible maximum of three.

"And the third person on the prize, who will that be?" I ask.

Sinclair smiles coyly and says nothing.

David Ewing Duncan is a freelance journalist. His last article for Technology Review was "Brain Boosters," in the July/August issue.

Letter to a Young Scientist

In his newly released memoir *Avoid Boring People*, James Watson laces autobiography with advice. In the following excerpt, he tells the story of his role in determining the structure of DNA.

By James Watson

I arrived in Cambridge in the fall of 1951 sensing a majesty of place and intellectual style unmatched anywhere in the world. The city's great university, reflecting almost 900 years of English history, is centered on the banks of the River Cam, whose modest waters move northeast across East Anglia to the market city of Ely. Ely's massive 12th-century cathedral had long towered over the vast flat fenland marshes that emptied into the still 40 miles of river from Cambridge to the shallow waters of the Wash, the estuary over which tides from the North Sea still roar twice daily. It was the draining over many centuries of the fens that created the rich agricultural fields and wealth of the great East Anglia estate owners. Their benefactions in return helped create along the "backs" of the Cam the many elegant student residences, dining halls, and chapels that already many centuries ago marked out Cambridge as a market city of extraordinary grace and beauty.

For most of its history, Cambridge University was highly decentralized, with teaching carried out exclusively by the residential colleges, among which Trinity was long the grandest, having enjoyed the matchless patronage of Henry VIII. In a room off the great court had lived the young Newton, whose greatest science was done in his 20s and 30s before he went up to London to be master of the mint.

Until the mid-18th century, the primary role of the colleges was to educate clergy for the Church of England, a mission carried out by fellows (dons) who were themselves required to remain unmarried while part of college life. Only in the 19th century did science become an important part of the Cambridge teaching scene. Charles Darwin's serious excitement about natural history and geology came from his exposure in the early 1830s to these disciplines at Christ's College. Over the next half-century, the responsibility for instruction increasingly shifted away from the colleges to newly created academic departments under university control. In 1871, the duke of Devonshire,

Henry Cavendish, donated funds for the creation of the Cavendish Laboratory and the appointment of the first Cavendish Professor: James Clerk Maxwell, whose eponymous equations first unified the dynamics of electricity and magnetism. Upon Maxwell's early death at age 49 in 1879, the 29-year-old John William Strutt (Lord Rayleigh), famed for his ideas on optics, became the second Cavendish Professor of Physics. In 1904, he was to win a Nobel Prize, as would the next four successors to the chair: J. J. Thomson (1906), Ernest Rutherford (1908), William Lawrence Bragg (1915), and Nevill Mott (1977).

By the start of the 20th century, Cambridge stood out as one of the world's leading centers for science, of the same rank as the best German universities—Heidelberg, Göttingen, Berlin, and Munich. Over the next 50 years, Cambridge would remain in that rarefied league, but Germany would be supplanted by the United States, much strengthened by its absorption of many of the better Jewish scientists forced to flee Hitler. England similarly benefited from the arrival of



Essay

some extraordinary Jewish intellectuals. If Max Perutz had not had the good sense to leave Austria in 1936 as a young chemist, there would have been no reason for my now moving to the banks of the Cam.

Though winning the great struggle against Hitler had drained England financially, the country's intellectuals took pleasure in knowing that victory had been much of their own making. Without the physicists who provided radar for British aviators during the Battle of Britain, or the Enigma code breakers of Bletchley Park who successfully pinpointed the German U-boats assaulting the Allies' Atlantic convoys, things might have turned out very differently.

Emboldened by the war to think expansively, the then tiny Medical Research Council (MRC) Unit for the Study of Structure of Biological Systems was doing science in the early 1950s that most chemists and biologists thought ahead of its time. Using x-ray crystallography to establish the 3-D structure of proteins was likely to be orders of magnitude more difficult than solving the structures of small molecules like penicillin. Proteins were daunting objectives, not only because of size and irregularity but because the sequence of the amino acids along their polypeptide chains was still unknown. This obstacle, however, was likely soon to be overcome. The biochemist Fred Sanger, working less than half a mile away from Max Perutz and John Kendrew at the MRC lab, was far along the path to establishing the amino acid sequences of the two insulin polypeptides. Others following in his steps would soon be working out the amino acid sequences of many other proteins.

Polypeptide chains within proteins were then thought to have a mixture of regularly folded helical and ribboned sections intermixed with irregularly arranged blocks of amino acids. Less than a year before I arrived in England, the nature of the putative helical folds was still not settled, with the Cambridge trio of Perutz, Kendrew, and Sir Lawrence Bragg hoping to find their way by building Tinkertoy-like, 3-D models of helically folded polypeptide chains. Unfortunately, they got a local chemist's bad advice about the conformation of the peptide bond and, in late 1950, published a paper soon shown to be incorrect. Within months they were upstaged by Caltech's Linus Pauling, then widely regarded as the world's best chemist. Through structural studies on dipeptides, Pauling inferred that peptide bonds have strictly planar configurations, and in April 1951, he revealed to much fanfare the stereochemically pleasing alpha helix. Though Cambridge was momentarily stunned, Max Perutz quickly responded using a clever crystallographic insight to show that the chemically synthesized polypeptide

polybenzylglutamate took up the alpha-helical conformation. Again the Cavendish group could view itself as a major player in protein crystallography.

The unit's resident theoretician was by then the physicist Francis Crick, who at 35 was two years younger than Max Perutz and one year older than John Kendrew. Francis was of middle-class, Nonconformist, Midlands background, though his father's long-prosperous shoe factories in Northampton failed during the Great Depression of the 1930s. It was only with the help of a scholarship from Northampton Grammar School that Francis moved to the Mill Hill School in North London, where his father and uncle had gone. There he liked science but never pulled out the grades required for Oxford or Cambridge. Instead he studied physics at University College London, afterwards staying on for a PhD financially sponsored by his Uncle Arthur, who after Mill Hill had chosen to open an antacid-dispensing pharmacy instead of joining the family shoe business.

Unlike Max and John, who came into science as chemists and now held PhDs, Francis had not completed his doctorate. He had done just two years of thesis research, winning a prize for his experimental apparatus to study the viscosity of water under high pressure and temperature, when the advent of the war moved him to the Admiralty. He joined the high-powered group set up to invent countermeasures against German magnetic mines, and in 1943, his boss, the Cavendish-trained nuclear physicist Harrie Massey, gave him the challenge of combating the German navy's latest innovation. In great secrecy, German shipyards had under construction a new class of mine sweepers (Sperrbrechers) whose bows were fitted with huge 500-ton electromagnets designed to trigger magnetic mines lying a safe distance ahead. Crick came up with the clever idea that a specially designed insensitive mine would not explode until a Sperrbrecher passed directly over it. By the end of the war, more than 100 Sperrbrechers were so sent to the bottom of the ocean.

After Harrie Massey left to lead the British uranium effort at Berkeley, the Cambridge mathematician Edward Collingwood became Francis's mentor. He saw Francis as both a friend and an invaluable colleague, inviting him for weekends to his large Northumbrian home, Lilburn Tower, and taking him to Russia in early 1945 to help decipher the workings of a just-captured German acoustic torpedo.

After the war's end, Francis's new bosses did not need to be as forgiving of his loud, piercing laughter or of the distaste for conventional thinking that often inspired it. Though formally made a member of the civil service in mid-1946, Francis soon lost interest in military intelligence and wanted a bigger challenge. He saw in biology the greatest range of potential problems to engage his inquisitive mind.

Apprised of Francis's desire for a radical change of course, Harrie Massey sent him along to see the physicist Maurice Wilkins at King's College London's new Biophysics Laboratory. After the war, while still in Berkeley, Massey had changed Wilkins's life by giving him a copy of Erwin Schrödinger's What Is *Life?* Its message that the secret of life lay in the gene was as compelling to Maurice as it had been to me, and he soon began to make his move into biophysics. He would join J. T. Randall at St. Andrews and then move with him to London. Immediately he and Francis became friends, with Maurice soon asking Randall to offer a job to Francis. Randall thought better of it, though, correctly seeing Francis as a mind he could not control. The Medical Research Council, mindful of Francis's high wartime repute, came to his rescue and funded his learning to work with cells at the Strangeways Laboratory on the outskirts of Cambridge.

His task during the next two years at the Strange-ways—observing how tiny magnets moved through the cytoplasm of cells—did not win Francis any kudos. At best it was busywork that gave him time to seek out more appropriate challenges. These at last came when he moved his MRC scholarship across Cambridge to Max Perutz's protein-crystallographic unit. Though his new job was no better paid, it would let him work toward the PhD, by then a prerequisite for meaningful academic positions.

By the time I came to Cambridge, Francis's forte was increasingly seen to be crystallographic theory, though his early forays in the field had not been universally appreciated. At his first group seminar in July 1950, entitled "The Theory of Protein Crystallography," he came to the conclusion that the methodologies currently used by Perutz and Kendrew could never establish the three-dimensional structure of proteins—an admittedly impolitic assertion that caused Sir Lawrence Bragg to brand Crick a boat rocker. Much more harm came a year later when Bragg presented his newest brainchild and Francis told him how similar it was to one he himself had presented at a meeting six months earlier. After the infuriating implication of his being an idea snatcher, Sir Lawrence called Francis into his office to tell him that once his thesis was completed he would have no future at the Cavendish. Fortunately for me, and even more so for Francis, Cambridge was unlikely to grant him the degree for another 18 to 24 months.



THE PARTNER Trained as a physicist, Francis Crick worked closely with James Watson to discover the structure of DNA.

I was by then having lunch with Francis almost daily at the nearby pub, the Eagle, which during the war was favored by American airmen flying out of nearby airfields. Soon we would be upgraded from desks beside our lab benches to a largish office of our own next to the connected pair of smaller rooms used by Max and John. There, Francis's ever irrepressible laughter would less disturb the work habits of other unit members. At our first meeting, Francis had spoken of his much valued friend Maurice Wilkins, who, like him, had made a wartime marriage that soon disintegrated with peace. Because he was curious to know whether Maurice's crystallography had generated any new, perhaps sharper x-ray photos from DNA, Francis invited him for a Sunday dinner at the Green Door, the tiny apartment on top of a tobacconist shop on Thompson Lane, across from St. John's College. Earlier occupied by Max Perutz and his wife Gisela, it had been home to Francis and his second wife Odile since their marriage two years before in August 1949.

At that meal, we learned of an unexpected complication to Maurice's pursuit of DNA. While he was on an extended winter visit to the United States, his boss, Professor J. T. Randall, had recruited to the King's DNA effort the Cambridge-trained physical chemist Rosalind Franklin. For the past four years she had been

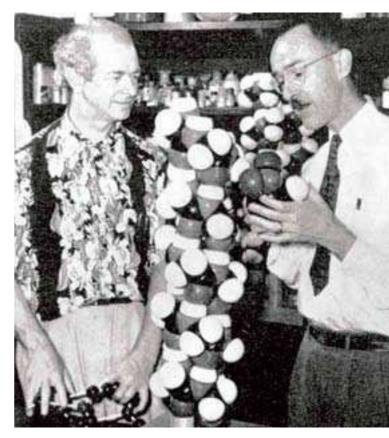
using x-rays in Paris to investigate the properties of carbon. Rosalind understood from Randall's description of her responsibilities that x-ray analysis of DNA was to be her responsibility solely. This effectively blocked Maurice's further x-ray pursuit of his crystalline DNA. Though not formally trained as a crystallographer, Maurice had already mastered many procedures and had much to offer. But Rosalind didn't want a collaborator; all she wanted from Maurice was the help of his research student Raymond Gosling. Now, though out in the cold for two months, Maurice could not stop thinking about DNA. He believed his past x-ray pattern did not arise from single polynucleotide chains but from helical assemblies of either two or three intertwined chains bonded to each other in a fashion as yet to be determined. With the DNA ball sadly no longer under his control, Maurice suggested that if Francis and I wanted to learn more we should go to King's in a month's time, November 21, to hear Rosalind give a talk.

Before it was time to go to London, Francis had reason to feel good about his place in the Cavendish. He and the clever crystallographer Bill Cochran derived easy-to-use mathematical equations for how helical molecules diffract x-rays. Each of them, in fact, did so independently within 24 hours of being shown by Bragg a manuscript from Vladimir Vand in Glasgow, whose equations they immediately saw as only half baked. Theirs was an important achievement, for Francis and Bill had given the world the equations that could predict the diffraction patterns of helices according to specific dimensions. The next spring I was to deploy them to show that the protein subunits of Tobacco Mosaic Virus are helically arranged.

The best way to reveal DNA's 3-D structure might well then have been through building molecular models using Cochran and Crick's equations. Until a year before, this approach had made no sense, since the nature of the covalent bonds linking nucleotides to each other in DNA chains was unknown. But after work by Alex Todd's nearby research group in the Chemical Laboratory at Cambridge, it was clear that DNA's nucleotides are held together by 3'-5' phosphodiester bonds. A focus on model building was a way to set oneself apart from the alternative approach of focusing on x-ray photograph details being pursued at King's College in London.

On the day of the lecture, Francis was unable to go down to London, and I went alone, still oblivious to the difference between the crystallographic terms "asymmetric unit" and "unit cell." As a result, the next morning I mistakenly reported to Francis that

Rosalind's DNA fibers contained very little water. My error only came to light a week later, when Rosalind and Maurice came up from London to look at a three-chain model that we had hastily constructed. It had DNA's sugar-phosphate backbone in the center with the bases facing outward. Upon seeing it, Rosalind immediately faulted its conception, saying the phosphate groups were located on the outside, not the inside, of the molecule. Moreover, we had proposed DNA to be virtually dry, whereas, in fact, it was highly hydrated. And we got the unmistakable impression



MEANWHILE ... In 1951, Caltech's Linus Pauling (left) and Robert Corey discovered the alpha helix, but they failed to figure out DNA.

that the King's group considered the pursuit of the DNA structure to be their property, not one to be shared with their fellow MRC unit in Cambridge. All too soon we learned that Sir Lawrence Bragg was of the same mind, when he told us to refrain from all subsequent DNA model-building activities. In stopping us Bragg was not motivated solely by a need to remain on good terms with another MRC-supported group. He wanted Francis to focus exclusively on research for his PhD and be done with it.

This debacle, however, would not have occurred if Francis and I had started to think as if we were chem-

ists. Even without the King's x-ray patterns, there were clues in the chemical literature that should have led us to propose a double helix as the basic structure of DNA. From the start we should have restricted ourselves to models in which externally located sugarphosphate backbones were held together by hydrogen bonds between centrally located bases. Strong physicalchemical evidence for bases so held together had come from the postwar experiments of John Gulland. In 1946, his Nottingham lab showed that within native DNA molecules the bases are so arranged as to hinder them from exchanging hydrogen atoms. These data suggested widespread hydrogen bonding between DNA bases. This insight was widely available, published by the Cambridge University Press in the 1947 SEB Symposium volume on nucleic acids.

Furthermore, given Linus Pauling and Max Delbrück's prewar proposal that the copying of genetic molecules would involve structures of complementary shape, Francis and I should have reasonably focused on two-chain rather than three-chain models. In a two-chain model, each DNA base would hydrogen-bond exclusively to one with a molecule of complementary shape. In fact, experimental data pointing to this conclusion, too, already had been published, most coming from the lab of the Austrianborn chemist Erwin Chargaff in New York. Without understanding the significance of his discovery, Chargaff reported that in DNA, the amounts of the purine adenine were roughly equal to the amounts of the pyrimidine thymine. Likewise, the amount of the second purine, guanine, was similar to the amount of the second pyrimidine, cytosine.

The exact shape of such base pairs would depend upon where the atoms available for hydrogen bonding were located on each base. In 1951, few chemists knew enough quantum mechanics to make such inferences. So that fall we should have sought advice from the several British chemists trained in this esoteric field. In retrospect, Alex Todd's lab, after determining the covalent linkages in DNA, should have moved on to determining what the molecule looks like in three dimensions. But in those days, even the best organic chemists thought such problems were better left to x-ray crystallographers. In turn, most x-ray diffraction experts felt the time had not yet arrived to tackle biological macromolecules. In a sense, then, the field was wide open.

Even after he found the alpha helix, Linus Pauling remained only moderately attentive to DNA, never seriously believing that it had a genetic role. Even so, when hearing of Maurice Wilkins's crystalline photo, he asked to have a look, being misinformed that Maurice himself was not seriously trying to determine the structure. As that was precisely what Maurice was up to, he quickly replied that he wanted more time to look over the photo before releasing it to others. Undeterred, Linus wrote directly to the King's boss, John Randall, but this approach was likewise unsuccessful. Linus lost the scent until a year later at a summer phage meeting outside of Paris, where he first learned of the work recently completed at Cold Spring Harbor by Alfred Hershey and Martha Chase, showing that phages were also made from DNA. The news convinced Linus he must go after the DNA structure despite his lack of high-quality DNA x-ray photos. His voyage back to the States could have been a great fortuitous opportunity. Also on board the transatlantic boat was Erwin Chargaff, who like Pauling had come to Europe to attend that summer's International Biochemical Congress in Paris. But instead of learning about the equivalence of A with T and G with C, Linus took an instantaneous dislike to his shipmate and avoided him all across the Atlantic.

Preoccupied much of the fall of 1952 with the race against Francis Crick for the coiled-coil structure of

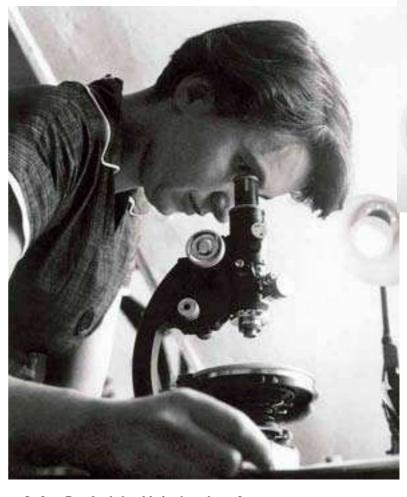
Even after he found the alpha helix, Linus Pauling remained only moderately attentive to DNA, never seriously believing that it had a genetic role.

alpha keratin, Pauling only turned to DNA in earnest in late November. Soon he was very much attracted to a DNA model in which three sugar-phosphate backbones coiled around each other. He was hung up on three chains because of the reported high density of DNA. At no time did he seriously consider a two-chain molecule. For the three chains to hold together, he reasoned, DNA would have to be uncharged, forming hydrogen bonds between opposing phosphate groups. Soon satisfied that he had found the general structure for nucleic acids, he wrote to Alex Todd a week before Christmas adding that he was not bothered that his structure provided no clues as to how DNA functions in cells. That problem was for another day. At no time did he ever take into account Chargaff's base compositions, published more than a year before in several journals. The essential parameters for Linus that December were bond angles and length, not what DNA did biologically or how it behaved in solution. It

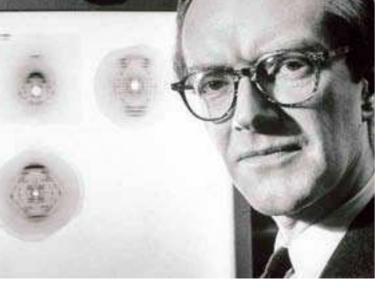
was immediately evident that the atoms of his model were not fitting together as neatly as they did in the alpha helix. Even his best structure was stereochemically shaky, with several central phosphate oxygens uncomfortably close to each other.

Fearing that someone in England might beat him to the punch with a similar model, Linus hastily submitted a manuscript for publication in the *Proceed*ings of the National Academy. Then he triumphantly sent two manuscript copies to Cambridge-one to Bragg, the other to his son, Peter. We were instantly engulfed in anxiety until we realized that Linus had used hydrogen atoms belonging to the phosphate groups to hydrogen-bond the three chains together. We knew at once that his model must be wrong, since DNA-an acid-normally releases all its hydrogen ions in solution. So Francis and I rushed around Cambridge to see whether the local chemical hotshots also found Pauling's concept totally implausible. Quickly reassured by Alex Todd that Linus had indeed made a gigantic chemical goof, I went down almost immediately to London to show the manuscript to Maurice Wilkins and Rosalind Franklin, the latter preparing to move to J. D. Bernal's group in Birkbeck College, where she would no longer work on DNA.

Maurice was more than relieved to learn that Linus was so far off base. In contrast, Rosalind was annoyed at my showing her the manuscript, tartly telling me that she had no need to read about helices. In her mind, the crystalline DNA A-form structure was most certainly not helical. In fact, six months before, she had sent out invitations to a July "memorial service" to celebrate the death of the DNA helix. Here Maurice thought that Rosalind had been badly deluding herself, and to prove it, he impulsively showed me an x-ray photo that the King's group had been keeping secret since Raymond Gosling took it more than nine months before. Originating from a more hydrated B-form DNA fiber, this picture displayed unequivocally the large cross-shaped diffraction pattern to be expected from a helical molecule. My jaw dropped, and I rushed back to Cambridge to tell everyone what I had learned. I thought we should not wait a moment longer before commencing to build models. Someone was bound to tell Linus that his was dead on arrival. Sir Lawrence Bragg instantly agreed, and with him finally behind us, Francis and I soon were back playing with cutout shapes. By then I realized that DNA's density did not, as I originally thought, rule out two strands as opposed to three. It thus made sense for me to focus first on possible ways for two DNA chains to twist around each other.



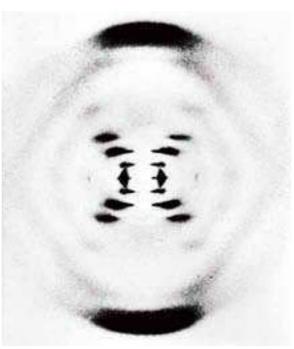
In fact, Rosalind should also have been focusing on two-chained DNA models. More than a year before, she had carefully measured her x-ray diffraction patterns from crystalline A-form DNA looking for possible molecular symmetries. Finding her data compatible with three possible chemical "space groups," she went up to Oxford to get advice from Dorothy Hodgkin, then England's premier crystallographer, justly famed for solving the structure of penicillin. As soon as Dorothy saw that Rosalind was considering space groups involving mirror symmetry, however, she sensed crystallographic callowness. Experienced crystallographers would never postulate mirror symmetry for a molecule made up exclusively of 2-deoxy-D-ribose. Instead, Dorothy believed, Rosalind should have been considering only the implications of the third monoclinic space group (a rectangular prism of three unequal axes). Upset by Dorothy's sharp put-down of her crystallographic acumen, Rosalind left Oxford, never to return. If she had gone instead to Francis for help, she would have immediately learned that the C2 monoclinic space group suggested that DNA was a double helix with its chains running in opposite directions.



"MY JAW DROPPED" An x-ray image of the B form of DNA (right) taken from Rosalind Franklin's laboratory convinced James Watson that DNA had a helical structure. The image was, unknown to Franklin (left), shown to Watson by Maurice Wilkins (above). Had Franklin and Wilkins gotten along better, they might have determined the structure of DNA first.

Francis only learned of DNA's monoclinic space group through reading a nonconfidential King's progress report sent to Max Perutz in mid-February. By then, through a new burst of model building, I had found that a sugar-phosphate backbone of 20-angstrom diameter optimally repeats every 34 angstroms, the repeat distance measured in B-form DNA. Francis now argued, in light of Rosalind's space group, that the two chains must run in opposite directions. But I didn't initially buy this assertion, not understanding the underlying crystallographic symmetry argument. Until I knew how the centrally located bases bonded to each other, I didn't want to worry about backbone directions. Then, unknown to me, my model building was being hindered by faulty textbook descriptions of the structures of guanine and thymine. Using such false configurations, I had become momentarily excited about a pairing scheme similar to that found in crystals of adenine.

That scheme, however, would have given a 17angstrom repeat along the helical axis, not the 34angstrom figure observed by Rosalind. Happily, the Caltech structural chemist Jerry Donohue, then spending his sabbatical year in Cambridge, set me on the right track by arguing that the guanine and thymine hydrogens should have keto rather than the textbookascribed enol configurations. Needing only a day to incorporate Jerry's reasoning, I changed the locations of the hydrogen atoms on my paper-cutout models of thymine and guanine. Almost instantly I found myself forming the A-T and G-C base pairs we now know to exist in DNA. Coming a half-hour later into our office that Saturday morning, Francis took only a few min-



utes to conclude that the symmetry of the base pairs demanded that the chains run in opposite directions. Rosalind's monoclinic space group was in a true sense a prediction of a model derived by Francis and me from purely stereochemical arguments. The double helix had to be correct. All that remained to be done was to build a backbone segment and measure its atomic coördinates to show that all the bond lengths and angles in our model agreed with those previously found in smaller molecules. This task, which for the first time in months took Francis away from his desk, took less than three days to complete. The double helix was ready to let loose upon the world.

Breaking the news to Wilkins that we very likely had solved the DNA structure was bound to cause his heart to spasm. A day after we had verified appropriate coördinates for all the atoms, a letter from him arrived informing Francis that Rosalind was out of King's and that Maurice was about to resume work on DNA. Perhaps to soften the blow, John Kendrew, not Francis, called Maurice to report that Francis and I had a promising novel structure for DNA. Coming up the next day, Maurice instantly recognized the double helices' elegant simplicity and agreed that it was likely too good not to be true. Knowing that we would not have found the DNA structure without knowledge of x-ray results from King's, Francis and I suggested to Maurice that his name also be on the manuscript we planned to send to *Nature*. Without hesitation, he declined, possibly not knowing how to deal with Rosalind Franklin's and Raymond Gosling's equally

important contributions. The April 25, 1953, issue of *Nature*, besides containing the 900-word description of our model, also included separate continuing contributions from the two warring DNA groups at King's. Maurice was later to write that his refusal to publish jointly with the two of us was the biggest mistake of his life.

In every sense, solving the double helix was a problem in chemistry. Alex Todd facetiously told me that Francis and I were good organic chemists, not wanting to admit that a major objective in chemistry had been solved by nonchemists. In reality, Francis and I would not have been first to see the structure if Todd's fellow chemists had not done botched jobs. Linus had all the keys to unlock the DNA structure but inexplicably didn't use them that fall of 1952. Rosalind Franklin would have seen the double helix first had she seen fit to enter the model-building race and been better able to interact with other scientists. If she had accepted rather than rejected Maurice as a collaborator, the two of them could not have failed to realize the significance of the monoclinic space group. Dorothy Hodgkin's Oxford put-down of Rosalind as a crystallographer would not have been the fatal wound that it seems in retrospect.

Two of the three big questions in molecular genetics, the DNA structure by which genetic information is carried and how it is copied, were thus suddenly resolved through the discovery of basepair hydrogen bonding.

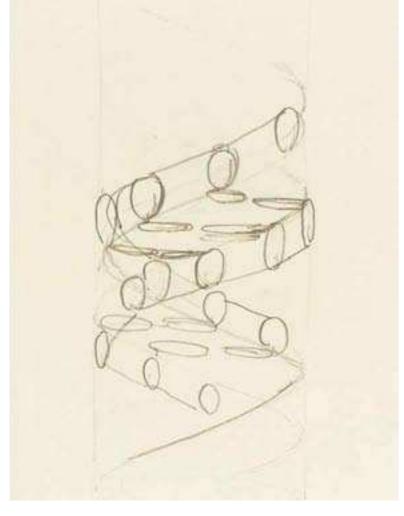
In contrast, Francis and I were far from being on our own. One flight up was the clever Bill Cochran, who put the Bessel functions of helical diffraction theory into Francis's working vocabulary, whence they entered mine. Even more important, Jerry Donohue's spartan desk was no more than 12 feet from mine and Francis's when his quantum chemistry expertise squelched my initial desire to build a double helix based on like-with-like base pairing (e.g., A-A and T-T). The Cavendish then was a magnet for minds that wanted to be challenged by others of equal power. In contrast, Linus Pauling's Caltech was a chemistry garden of mortals hovered over by a god who saw no need to assimilate

the ideas and facts of others. If Linus had only spent a few days in Caltech's libraries perusing the literature on DNA that fall, he would most likely have hit upon the idea of base pairing and would now be celebrated for both the alpha helix and the double helix.

Virtually everyone who came to our now even more cramped Cavendish office to see the large 3-D model made in early April was thrilled by its implications. Any doubt as to whether DNA, and not protein, was the genetic information-bearing molecule suddenly vanished. The complementary nature of the base sequences on the opposing chains of the double helix had to be the physical counterpart of the Pauling-Delbrück theoretical postulation of gene copying through the creation of complementary intermediates. DNA double helices as they exist in nature must reflect single-stranded template chains hydrogen-bonded to their single-stranded products of complementary sequence. Two of the three big questions in molecular genetics, the DNA structure by which genetic information is carried and how it is copied, were thus suddenly resolved through the discovery of base-pair hydrogen bonding.

Still to be ascertained was how the information conveyed by the sequence of DNA's four bases (adenine, guanine, thymine, and cytosine) determines the order of the amino acids in the polypeptide products—the stuff of the proteins forming all living things-of individual genes. Since there were known to be 20 amino acids and only four DNA bases, groups of several bases must be used to specify, or code for, a single amino acid. I initially thought the language of DNA would be best approached not through further work on the DNA structure but by work on the 3-D structure of its close chemical relative ribonucleic acid (RNA). My decision to move on from DNA to RNA reflected the already several-years-old observation that polypeptide (protein) chains are not assembled on DNA-containing chromosomes. Instead, they are made in the cytoplasm on small RNA-containing particles called ribosomes. Even before we found the double helix, I postulated that the genetic information of DNA must be passed on to RNA chains of complementary sequences that in turn function as the direct templates for polypeptide synthesis. Naively, I then believed that amino acids bonded to specific cavities linearly located on the surfaces of the ribosome RNA components.

After three subsequent years of x-ray studies—the first two at Caltech and the last back with the "unit" in Cambridge, England, in which I was joined by the Pauling- and Harvard Medical School-trained Alex Rich—I failed to generate a plausible 3-D structure



STILL LIFE Francis Crick's 1953 pencil sketch of the double helix

for RNA. Though RNA from many different sources produced the same general x-ray diffraction pattern, the pattern's diffuse nature gave no solid clues as to whether the underlying RNA structure contained one or two chains. By early 1956, I decided to change my focus from x-ray studies on RNA to biochemical investigations on ribosomes when I returned to the States to begin teaching in the fall at Harvard. Also then seeking a more tractable challenge was the Swiss-born biochemist Alfred Tissières, then studying oxidative metabolism at the Molteno Institute in Cambridge. He had already briefly dabbled with ribosomes from bacteria and liked the idea of our seeking out how they work across the Atlantic in the other Cambridge.

Alfred came from an old Valais family that long owned a bank in Sion. When he was less than a year old his banker father tragically died during the great influenza epidemic of 1918. Much later a minor inheritance let Alfred buy the sleek Bentley that he parked across the Cam on land adjacent to the school for the famed King's College boys' choir. An even greater source of pride than his car was Albert's election to the British Alpine Club in 1950. His formidable ascents of the south face of the Taschhorn and the north ridge of the Dent Blanche led to an invitation to join the 1951 Swiss Everest reconnaissance expedition. Regretfully, he had to decline, giving priority to his research efforts in the Molteno Institute that led, in 1952, to a research fellowship at King's. Climbing, however, always remained essential to his psyche. In the summer of 1954 he joined in the Alpine Club's reconnaissance of Pakistan's Rakaposhi, at almost 8,000 meters high one of the Karakoram's most daunting peaks.

Francis was keenly awaiting the arrival of my successor as the unit's geneticist, the South African-born Sydney Brenner. We first met when he was working for a PhD at Oxford following medical training in Johannesburg. In the spring of 1953, Sydney was among those to have come to Cambridge to have a peek at our big molecular model of the double helix. He entered our lives more importantly, however, during the summer of 1954, when Francis and I were at Woods Hole on Cape Cod, talking genetic codes with the Russian-born big-bang theoretical physicist George Gamow. Then learning bacterial genetics at Cold Spring Harbor, Sydney came to Woods Hole for several days, greatly impressing Gamow and Francis by his quickness to catch on to their ideas and to propose experiments to test them.

Gamow, then a professor at George Washington University, was first drawn to the double helix in the summer of 1953, when he read our second Nature paper on the subject ("Genetical Implications of the Structure of DNA"). By early 1954, some of his seemingly wacky initial ideas had crystallized into a precise mechanics for the genetic code by which overlapping groups of three nucleotides coded for successive amino acids along polypeptide chains. On an early May 1954 visit to Berkeley, where George was on sabbatical, I proposed that we form a 20-person code-seeking club, one member for every amino acid. George instantly reacted positively, much anticipating designing a tie and stationery for our RNA Tie Club.

Though there was never a convention of all its members, "notes" that circulated among the RNA Tie Club greatly advanced thought about genetic codes. The most famous of these notes, by Francis, in time would totally change the way we thought about protein synthesis. In January 1955, Francis wrote to the club correctly suggesting that amino acids, prior to being incorporated in polypeptide chains, would attach to small RNA adaptors that in turn bind to template RNA molecules. For each amino acid, Francis postulated, there must exist a specific adaptor RNA (now called transfer RNA). In the absence of any experimental evidence for small RNA, much less their chemical binding to amino acids, even Francis could not long remain buoyant about his "adaptors." Six months were to pass

93

before he was to regain a manic mood, but this time it was over a 3-D model for collagen that he and Alex Rich built over the summer of 1955.

Alex returned in December to his job at the National Institutes of Health outside Washington, DC, and Francis and I focused for the winter of 1956 on the structures of small spherical RNA viruses, outlining how their cubic symmetry resulted from the regular aggregation of smaller asymmetrical protein building blocks. How their single, long RNA chains were organized with their polyhelical protein shells remained to be seen. Our last time as a team of two was at a Johns Hopkins University–organized symposium in midJune 1956, entitled "The Chemical Basis of Heredity." Upon arriving at the Hotel Baltimore, Francis jubilantly pointed out that we had been assigned adjacent rooms in the top-floor presidential suite.

After that occasion, staying at the top was to be a challenge we would have to face separately.

Remembered Lessons

1) Choose an objective apparently ahead of its time Mopping up the details after a major discovery has been made by others will not likely mark you out as an important scientist. Better to leapfrog ahead of your peers by pursuing an important objective that most others feel is not for the current moment. The threedimensional structure of DNA in 1951 was such an objective, regarded by virtually all chemists as well as biologists as unripe. One well-known scientist then toiling in DNA chemistry predicted that 100 years would pass before we knew what the gene looked like at the chemical level. Before setting out, you need to figure out a new path by which to climb—or even better, a new intellectual catapult that can potentially hurl you over crevasses seemingly too broad to be leapt over by experimentation. The model-building approach to the DNA structure in 1951 had the potential to let us get where we needed to go at a time when the more orthodox approach of analyzing x-ray diagrams was far from straightforward. Given Pauling's recent success using molecular modeling to find the alpha helix, using this approach on DNA was far from outlandish; actually, it was a no-brainer.

2) Only work on problems when you feel tangible success may come in several years

Many big goals are truly ahead of their time. I, for one, would like to know now where exactly my home telephone number is stored in my brain. But none of my colleagues who think about the brain yet know even

how to approach this problem. We might do very well by asking how the cells in the much, much smaller fly brain are wired so as to recognize the odor of a specific alcohol—that would be getting us somewhere.

I only feel comfortable taking on a problem when I feel meaningful results can come over a three- to five-year interval. Risking your career on problems when you have only a tiny chance of seeing the finish line is not advisable. But if you have reason to believe you have a 30 percent chance of solving over the next two or three years a problem that most others feel is not for this decade, that's a shot worth taking.

3) Never be the brightest person in a room

Getting out of intellectual ruts more often than not requires unexpected intellectual jousts. Nothing can replace the company of others who have the background to catch errors in your reasoning or provide facts that may either prove or disprove your argument of the moment. And the sharper those around you, the sharper you will become. It's contrary to human, and especially to human male, nature, but being the top dog in the pack can work against greater accomplishments. Much better to be the least accomplished chemist in a super chemistry department than the superstar in a less lustrous department. By the early 1950s, Linus Pauling's scientific interactions with fellow scientists were effectively monologues instead of dialogues. He wanted adoration, not criticism.

4) Stay in close contact with your intellectual competitors In pursuing an important objective, you must expect serious competition. Those who want problems to themselves are destined for the backwaters of science. Though knowing you are in a race is nerve-racking, the presence of worthy competitors is an assurance that the prize ahead is worth winning. You should feel more than apprehensive, however, if the field is too large. This usually means you are in a race for something too obvious, not enough ahead of its time to deter the more conservative and less imaginative majority. The presence of more than three or four competitors should tell you that your chance of winning is not only low but virtually incalculable, since you are unlikely to have a detailed knowledge of the strengths and weaknesses of most of your competition. The smaller the field, the better you can size it up, and the better the chance you will run an intelligent race.

Avoiding your competition because you are afraid that you will reveal too much is a dangerous course. Each of you may profit from the other's help, and an effective dead heat that allows you to publish simul-



FANFARE Nobel Prize ceremony, 1962. Left to right: Wilkins, Max Perutz, Crick, John Steinbeck, Watson, John Kendrew.

taneously is obviously preferable to losing. And if it happens that someone else does win outright, better it be someone with whom you are on good terms than some unknown competitor whom you will find it hard not to at least initially detest.

5) Work with a teammate who is your intellectual equal Two scientists acting together usually accomplish more than two loners each going his or her own way. The best scientific pairings are marriages of convenience in that they bring together the complementary talents of those involved. Given, for example, Francis's penchant for high-level crystallographic theory, there was no need for me to also master it. All I needed were its implications for interpreting DNA x-ray photographs. The possibility, of course, existed that Francis might err in some fashion I couldn't spot, but having kept good relations with others in the field outside our partnership, he would always have his ideas checked by others with even more crystallographic talents. For my part, I brought to our two-man team a deep understanding of biology and a compulsive enthusiasm for solving what proved to be a fundamental problem of life.

An intelligent teammate can shorten your flirtation with a bad idea. For all too long I kept trying to build DNA models with the sugar-phosphate backbone in the center, convinced that if I put the backbone on the outside, there would be no stereochemical restriction on how it could fold up into a regular helix. Francis's scorn for this assertion made me reverse course much sooner than I would have otherwise. Soon I too realized that my past argument had been lousy and, in fact, that the stereochemistry of the sugar-phosphate groups would of course move them to outer positions of helices that use approximately 10 nucleotides to make a complete turn.

In general, a scientific team of more than two is a crowded affair. Once you have three people working on a common objective, either one member effectively becomes the leader or the third person eventually feels a less-than-equal partner and resents not being around when key decisions are made. Threeperson operations also make it hard to assign credit. People naturally believe in the equal partnerships of successful duos-Rodgers and Hammerstein, Lewis and Clark. Most don't believe in the equal contributions of three-person crews.

6) Always have someone to save you

In trying to be ahead of your time, you are bound to annoy some people inclined to see you as too big for your britches. They will take delight if you stumble, believing your reversals of fortune are deserved. They may reveal themselves only in the moment of your discomfiture: often you find them controlling your immediate life by, say, determining whether you will get your fellowship or grant renewed. So it always pays to know someone of consequence-other than your parents—who is on your side. My hopes to go for broke with DNA by going to Cambridge would have come to nothing if my phage-day patrons, Salvador Luria and Max Delbrück, had not come to my rescue when my request to move my fellowship from Copenhagen to Cambridge was turned down. I was then judged, not without cause, to be unprepared for x-ray crystallography and urged to move instead to Stockholm to learn cell biology. Immediately, John Kendrew offered me a rent-free room in his home while Luria, through a personal connection, got my fellowship extended for eight months. Soon after, Delbrück arranged a National Foundation for Poliomyelitis fellowship for the succeeding year. In finding the funds that kept me in Cambridge, Luria and Delbrück were hoping that my new career as a biological structural chemist would be successful and do them proud. But they fretted about my being too far from their fold, knowing that I would likely leave empty-handed from my long Cambridge stay. The second year of my fellowship was, in fact, to be spent at Caltech, giving me at least a measure of security in the event the DNA structure was solved by others. In leaving one field for another, you should never burn your past intellectual bridges, at least until your new career has taken off. IR

James Watson's Avoid Boring People: And Other Lessons from a Life in Science will be published by Knopf in September.

95



Careers in Motion

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Career Growth Profile

ichael Moran had spent nearly a decade in the U.S. Navy when he realized that his future lay somewhere in the civilian world. As Moran saw it, his opportunities in the military were limited. But in the corporate sector, the sky was the limit. Though he was an officer who had gained a wide breadth of experience and respect, Moran knew that the road to corporate America would be a difficult one.

"If you were a lawyer, physician, or dentist in the military, then you had skills that were directly transferable to civilian life," Moran explains. "But I was a warfighter, and those skills, in the eyes of hiring managers, weren't transferable. In my discussions with recruitment agencies, I made the observation that I needed an MBA to gain credibility in the corporate sector."

At the time Moran decided to go back to school, he was stationed in Oahu, HI. He worked 55 to 65 hours a week, leading a staff of 22 at the Naval Computer and Telecommunications Area Master Station. His division oversaw programs that supported voice, video, and data communications for military operations in the Pacific area. The naval officer knew it would be a challenge to add graduate school to his calendar, but he didn't see any way around it.

"You make a decision, you engage, and you just put one foot in front of the other," says Moran, who earned an MBA with an emphasis in management information



MICHAEL MORAN

Age: 41

Job Title: Sr. Product Marketing Manager

Emphasis in information management

Employer: Initiate Systems **Program:** MBA, University of Hawaii

systems from the University of Hawaii. "What helped significantly was that my wife decided to pursue her master's degree in accountancy at the same time. My spouse understood exactly what I was going through, so it minimized the friction there. We were like two ships passing in the night most of the time."

For two and a half years, Moran took two courses a semester. Classes were held in the evenings on either a Tuesday-Thursday or a Monday-Wednesday-Friday schedule.

"The days I had class, I'd go straight from work; many times I'd end up going to class in my uniform," Moran recalls. "I'd start my day at 5 A.M. and wouldn't get home until 11:30 at night because there was a bit of a commute."

Looking back, Moran says it's hard to quantify how much time he spent studying outside of class, but he estimates it was about 20 to 30 hours a week.

"I'll be honest; there was hardly any downtime, but

this was something my wife and I both wanted to do to make these transitions in our lives," he says. "And I knew I needed to do the best I could to get the highest GPA. It was important that I really learn the material so I could be conversant when it came time to face the hiring managers."

While experiences can differ depending on the university and the program, Moran says a fair characterization of his graduate-school experience is that there was little "hand-holding" from the professors.

"You're given a syllabus and you're expected to do the reading and preparation outside of class; you either do the work or you don't," he says. "The university staff was excellent, but they were really more there to answer questions you might have or to help you better understand how to apply your knowledge."

Moran, who knew early in his life that he would join the navy, had little to no traditional business schooling when he entered the MBA program.

"For me, graduate school was an introduction into the business world," he says. "I was taking economics courses for the first time in my life. Unlike undergraduate school, the coursework was very practical in nature. To lean how Moran put his new skill-set to use outside of the classroom, visit www.technologyreview.com/resources/career/

Ask the Expert

Anne Drapeau, chief people officer at VistaPrint USA, has over 15 years of experience in human resources.

Q: How can I increase the odds of getting my employer to support my continuing education?

A: You might be lucky enough to work for a company that offers flextime, tuition reimbursement, and other benefits to employees who want to continue their education. Before you can receive these benefits, however, you'll probably need to justify why the company should invest in your education. Anne offers some advice on how to put together a convincing argument.

To read Anne's expert advice, visit www.technologyreview.com/career/resources

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Program Directory



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Reviews

Reviews

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ARTIFICIAL INTELLIGENCE

Higher Games

On the 10th anniversary of Deep Blue's triumph over Garry Kasparov in chess, a prominent philosopher of mind asks, What did the match mean? By Daniel C. Dennett

GARRY KASPAROV VS.

IBM'S DEEP BLUE

SUPERCOMPUTER

www.research.ibm.com/

May 1997

deepblue/

n the popular imagination, chess isn't like a spelling bee or Trivial Pursuit, a competition to see who can hold the most facts in memory and consult them quickly. In chess, as in the arts and sciences, there is plenty of room for beauty, subtlety, and deep originality. Chess requires brilliant thinking, supposedly the one feat that would be—

forever—beyond the reach of any computer. But for a decade, human beings have had to live with the fact that one of our species' most celebrated intellectual

summits—the title of world chess champion—has to be shared with a machine, Deep Blue, which beat Garry Kasparov in a highly publicized match in 1997. How could this be? What lessons could be gleaned from this shocking upset? Did we learn that machines could actually think as well as the smartest of us, or had chess been exposed as not such a deep game after all?

The following years saw two other human-machine chess matches that stand out: a hard-fought draw between Vladimir Kramnik and Deep Fritz in Bahrain in 2002 and a draw between Kasparov and Deep Junior in New York in 2003, in a series of games that the New York City Sports Commission called "the first World Chess Champi-

onship sanctioned by both the Fédération Internationale des Échecs (FIDE), the international governing body of chess, and the International Computer Game Association (ICGA)."

The verdict that computers are the equal of human beings in chess could hardly be more official, which makes the caviling all the more pathetic.

The excuses sometimes take this form: "Yes, but machines don't play chess the way human beings play chess!" Or sometimes this: "What the machines

do isn't *really* playing chess at all." Well, then, what *would* be really playing chess?

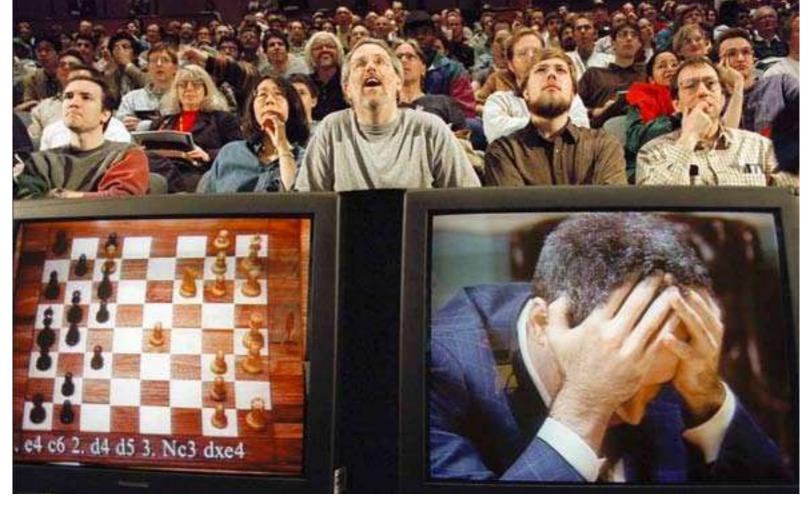
This is not a trivial question. The best computer chess is well nigh indistinguishable from the best human chess, except for one thing: computers don't know when to accept a draw. Computers-at least currently existing computers-can't be bored or embarrassed, or anxious about losing the respect of the other players, and these are aspects of life that human competitors always have to contend with, and sometimes even exploit, in their games. Offering or accepting a draw, or resigning, is the one decision that opens the hermetically sealed world of chess to the real world, in which life is short

and there are things more important than chess to think about. This boundary crossing can be simulated with an arbitrary rule, or by allowing the computer's handlers to step in. Human players often try to intimidate or embarrass their human opponents, but this is like the covert pushing and shoving that goes on in soccer matches. The imperviousness of computers to this sort of gamesmanship means that if you beat them at all, you have to beat them fair and square—and isn't that just what Kasparov and Kramnik were unable to do?

Yes, but so what? Silicon machines can now play chess better than any protein machines can. Big deal. This calm and reasonable reaction, however, is hard for most people to sustain. They don't like the idea that their brains are protein machines. When Deep Blue beat Kasparov in 1997, many commentators were tempted to insist that its brute-force search methods were entirely unlike the exploratory processes that Kasparov used when he conjured up his chess moves. But that is simply not so. Kasparov's brain is made of organic materials and has an architecture notably unlike that of Deep Blue, but it is still, so far as we know, a massively parallel search engine that has an outstanding array of heuristic pruning techniques that keep it from wasting time on unlikely branches.

True, there's no doubt that investment in research and development has a different profile in the two cases; Kasparov has methods of extracting good design principles from past games, so that he can recognize, and decide to ignore, huge portions of the





branching tree of possible game continuations that Deep Blue had to canvass seriatim. Kasparov's reliance on this "insight" meant that the shape of his search trees-all the nodes explicitly evaluated-no doubt differed dramatically from the shape of Deep Blue's, but this did not constitute an entirely different means of choosing a move. Whenever Deep Blue's exhaustive searches closed off a type of avenue that it had some means of recognizing, it could reuse that research whenever appropriate, just like Kasparov. Much of this analytical work had been done for Deep Blue by its designers, but Kasparov had likewise benefited from hundreds of thousands of person-years of chess exploration transmitted to him by players, coaches, and books.

It is interesting in this regard to contemplate the suggestion made by Bobby Fischer, who has proposed to restore the game of chess to its intended rational purity by requiring that the major pieces be *randomly* placed in the back row at the start of each game (randomly, but in mirror image for black

and white, with a white-square bishop and a black-square bishop, and the king between the rooks). Fischer Random Chess would render the mountain of memorized openings almost entirely obsolete, for humans and machines alike, since they would come into play much less than 1 percent of the time. The chess player would be thrown back onto fundamental principles; one would have to do more of the hard design work in real time. It is far from clear whether this change in rules would benefit human beings or computers more. It depends on which type of chess player is relying most heavily on what is, in effect, rote memory.

The fact is that the search space for chess is too big for even Deep Blue to explore exhaustively in real time, so like Kasparov, it prunes its search trees by taking calculated risks, and like Kasparov, it often gets these risks precalculated. Both the man and the computer presumably do massive amounts of "brute force" computation on their very different architectures. After all, what do neurons know about chess?

World chess champion Garry Kasparov during his sixth and final game against IBM's Deep Blue in 1997. He lost in 19 moves.

Any work *they* do must use brute force of one sort or another.

It may seem that I am begging the question by describing the work done by Kasparov's brain in this way, but the work has to be done somehow, and no way of getting it done *other* than this computational approach has ever been articulated. It won't do to say that Kasparov uses "insight" or "intuition," since that just means that Kasparov himself has no understanding of how the good results come to him. So since nobody knows how Kasparov's brain does it-least of all Kasparov himselfthere is not yet any evidence at all that Kasparov's means are so very unlike the means exploited by Deep Blue.

People should remember this when they are tempted to insist that "of course" Kasparov plays chess in a way entirely different from how a computer plays the game. What on earth could provoke someone to go out on a limb like that? Wishful thinking? Fear?

Reviews

In an editorial written at the time of the Deep Blue match, "Mind over Matter" (May 10, 1997), the New York Times opined:

The real significance of this overhyped chess match is that it is forcing us to ponder just what, if anything, is uniquely human. We prefer to believe that something sets us apart from the machines we devise. Perhaps it is found in such concepts as creativity, intuition, consciousness, esthetic or moral judgment, courage or even the ability to be intimidated by Deep Blue.

The ability to be intimidated? Is that really one of our prized qualities? Yes, according to the *Times*:

Nobody knows enough about such characteristics to know if they are truly beyond machines in the very long run, but it is nice to think that they are.

Why is it nice to think this? Why isn't it just as nice-or nicer-to think that we human beings might succeed in designing and building brainchildren that are even more wonderful than our biologically begotten children? The match between Kasparov and Deep Blue didn't settle any great metaphysical issue, but it certainly exposed the weakness in some widespread opinions. Many people still cling, white-knuckled, to a brittle vision of our minds as mysterious immaterial souls, or-just as romantic-as the products of brains composed of wonder tissue engaged in irreducible noncomputational (perhaps alchemical?) processes. They often seem to think that if our brains were in fact just protein machines, we couldn't be responsible, lovable, valuable persons.

Finding that conclusion attractive doesn't show a deep understanding of responsibility, love, and value; it shows a shallow appreciation of the powers of machines with trillions of moving parts. TR

Daniel Dennett is the codirector of the Center for Cognitive Studies at Tufts University, where he is also a professor of philosophy.

ENERGY

Electric Cars 2.0

Plug-in hybrids could bring gas-free commutes. But will they make it to market? By Kevin Bullis

A123 SYSTEMS'

LITHIUM-ION BATTERY www.a123systems.com

AUTOMOTIVE

t's a hot and smoggy day in Washington, DC, and things aren't going well for Les Goldman, a longtime energy lobbyist whose latest project is a new kind of car that is supposed to slash gasoline consumption and reduce greenhouse-gas emissions. We're outside his office, a block from the White House and a quick trip down Pennsylvania Avenue from Capitol Hill. And Goldman is sweating at the back of the "plug-in" hybrid that I'm supposed to test-drive, checking electrical connections and trying to figure out why it isn't working.

The car is a modified Toyota Prius with an extra battery installed in the spare-tire compartment. Conventional

hybrids like the Prius run on an electric motor part of the time, but the electricity they use is generated by a gasoline engine and by

capturing energy from braking. In the plug-in version of the car, the extra battery can be recharged from an electrical outlet. The battery stores about 40 miles' worth of electricity; if it's depleted, the car reverts to conventional hybrid mode.

The few plug-in vehicles on the road today are prototypes that, as Goldman is discovering, aren't always reliable. But recent advances in battery technology have attracted the attention of major manufacturers, raising the possibility of a mass-produced plug-in car. General Motors has announced that it is developing plug-in hybrids that use advanced lithium-ion batteries and could be ready within a few years. One of the GM designs-for a car known as the Volt-calls for a gasoline engine that kicks in after 40 miles just to recharge the battery. Toyota also

says it is researching lithium-ion batteries and testing plug-in vehicles.

An electric battery with a 40-mile range could nearly eliminate trips to the gas station for many drivers, since Americans drive just over 30 miles a day on average. But unlike earlier, allelectric cars, the new hybrids could handle longer commutes; the Volt is designed to travel 600 miles using its backup gas tank to charge the battery. And electricity from the grid is cheap: the equivalent of a gallon of gas costs less than a dollar.

The environmental arithmetic is also favorable. Generating the electricity to power plug-in cars causes less greenhouse-gas pollution than burn-

> ing gasoline does, accord-Electric Power Research Institute and the National Resources Defense Coun-

> ing to a recent study by the

cil. Even in the worst-case scenario, in which a plug-in vehicle got all its electricity from coal-fired plants (in reality, electricity in the United States comes from a mix of sources that on average release less carbon dioxide than coal plants do), it would still be responsible for a third less greenhouse-gas pollution than a conventional car. And though plug-ins and conventional hybrids would account for similar amounts of greenhouse-gas emission in most parts of the country, plug-ins in areas with clean sources of electricity, such as hydroelectric power, would be responsible for about half the carbon dioxide emissions of other hybrids.

Unlike other alternative technologies, such as cars powered by hydrogen fuel cells, plug-ins don't require any significant new infrastructure. Existing gas stations would provide the fuel



David Vieau, CEO of A123 Systems, shows President Bush a converted Toyota Prius. A123's batteries, which can be recharged from a standard electrical outlet, allow the car to travel farther on electricity alone.

for long trips, and electrical outlets in garages would provide the power for short commutes. (Eventually, charging stations could be installed for city dwellers.) And plenty of electricity is available, particularly overnight. According to a study from the Pacific Northwest National Laboratory, there's already enough excess generating capacity at night to charge 84 percent of the cars, pickups, and SUVs on the road today, if they were all suddenly converted into plug-in hybrids.

Better Batteries

A couple of weeks after my ill-fated attempt to test-drive the plug-in car in Washington, I'm outside the headquarters of battery maker A123 Systems in Watertown, MA. Out front is the shiny, aggressively styled GM Volt. The car is there because GM has selected A123 as one of two companies that could end up providing the battery technology for the Volt.

A123 makes a new type of lithiumion battery. Lithium-ion batteries,

which are now used widely in laptops and cell phones, pack a lot of energy into a small space. They take up just one-sixth the space of the lead-acid batteries used in previous types of electric vehicles, and they weigh one-sixth as much. They also take up less than half the space of nickel-metal hydride batteries, the kind used in today's conventional hybrids, while weighing just a third as much.

But the type of lithium-ion battery that's used in laptops and cell phones has problems, including the occasional tendency to overheat and, in rare cases, burst into flame. Troubling as this instability is in personal electronics, it could be even worse in a car, which uses a module that consists of hundreds of times the number of batteries found in an electronic device. On top of that, although prices have been coming down gradually, lithium-ion batteries are still expensive.

All that could change as a result of A123's batteries, in which electrodes based on cobalt oxide have been replaced with iron phosphate electrodes. At relatively low temperatures, oxides release oxygen, which can drive reactions that might heat up a battery and cause it to explode. But phosphates

Reviews

continue clinging to oxygen at much higher temperatures. What's more, iron is far cheaper than cobalt.

Volt or Bolt?

There is a giant "if" in all this, though. To become practical and economically viable, plug-in vehicles will need to be mass-produced.

Will automakers follow through on their highly publicized announcements about plug-ins? GM, for one, has a reputation for quitting on innovative engineering; the company's executives scrapped an earlier all-electric vehicle. And even though GM had an early lead in conventional hybrid technology, it failed to bring hybrids to market until after the success of Toyota's Prius. What will happen to plug-in plans if gas prices drop, or if interest in reducing greenhouse gases wanes?

No one can predict the results of the carmakers' fickle decision-making process. But a few things are clear. Plugins are the most practical and enticing alternative to the internal-combustion engine that has been developed in years. And their fate will depend on whether automakers learn from the success of conventional hybrids and fully embrace the new technology.

I did at last drive a working plug-in. The converted car glided noiselessly along the streets of Boston as I eyed a gauge that estimated my mileage at more than 150 miles per gallon. But on the day that I saw the Volt on display at A123's offices, GM wasn't giving rides; the car was just a mock-up, without the new batteries. As I sat in the driver's seat and grasped the steering wheel, sunlight streaming through the clear roof, it was easy to believe that plugins are on the way. But the mock-up was also a harsh reminder that when it comes to green innovation, U.S. automakers have long been more eager to show off flashy concept cars than to manufacture vehicles that work.

Kevin Bullis is the nanotechnology and materials science editor at Technology Review.



INTELLECTUAL PROPERTY

Patent Law Gets Saner

The U.S. Supreme Court has sent a clear message to "patent trolls": your paydays are numbered. By Scott Feldmann

EBAY V.

TELEFLEX

MERCEXCHANGE;

KSR INTERNATIONAL V.

MEDIMMUNE V. GENENTECH;

weighs in on patent law, so three of its recent decisions are noteworthy—and may even be historic. In effect, they address some unintended consequences of the 1982 act of Congress that created a new patent appellate court, the Federal Circuit, which brought uniformity to patent law and reduced the likelihood that a patent

would be found "invalid." Before 1982, there was always the risk that a prospective licensee would make a preëmptive strike, filing suit in a jurisdiction

that routinely found patents to be "obvious" and therefore invalid. This correction spurred investments in technology and an increase in patenting to protect them. But over the past several years, the patent system's high transaction costs have threatened to offset its benefits.

Established businesses have hotly argued that the patent system needs reform. Some charge that the U.S. Patent and Trademark Office is a major problem: because patent examiners are in short supply *and* have an evaluation system that favors allowances over rejections, unworthy patents are granted. But the angriest complaints are about unscrupulous patent-licensing compa-

nies—known as "trolls"—that aggressively seek licensing fees.

Good patent-licensing companies have long helped individuals and small companies get compensation for their inventions. Trolls are different. They send demand letters to thousands of putative patent infringers, often without doing their due diligence. They sometimes file suits against dozens of

> defendants, or in jurisdictions viewed as friendly to plaintiffs. Legislation limiting such suits to jurisdictions where the defendants are located or do business,

or where infringement has occurred, has gone nowhere. Some trolls will pull the trigger on everyone in sight and let the grind of litigation soften up the defendants for settlement, the merits of the cases be damned.

It wasn't always like this. Until 25 years ago, most companies obtained patents to prevent competitors from copying their significant new inventions. Aggressive use of patents to sue others was infrequent, since having a patent declared invalid was a significant risk; former Supreme Court justice William O. Douglas, for example, wanted "inventive genius" to remain the standard for validity. Things

Over the course of one year, the U.S. Supreme Court has heard three cases involving patent law. That's unusual.

changed significantly with the advent of the Federal Circuit. Previously, many appellate courts viewed patents as archaic and undesirable monopolies. But with patents more likely to be found valid, companies began to assert them. Technology-focused companies began demanding license fees under the implicit threat of litigation. Texas Instruments, for instance, garnered more than \$1 billion in licensing fees.

In response, large companies bulked up their patent portfolios to ensure that any lawsuit by a competitor would result in patent infringement counterclaims. That put everyone on edge. After all, a successful claim concerning any one of hundreds or thousands of patents in a company's portfolio could result in a patent injunctiona commandment by a judge to stop making, using, or selling goods or services infringing a patent. Having a war chest of patents gave a company leverage, and the possibility of negotiating a cross-license if a competitor sued. Then, in 1998, the Federal Circuit held that business methods could be patented. A flood of patent applications, some based on simple improvements in business operations, ensued. Many, because they were "obvious," should have been denied but were not.

Trolls noticed all this—as well as the fact that some jurisdictions were very friendly to patent holders. Jurisdictions whose jurors favor strong private-property rights were more inclined to find infringement; in the Eastern District of Texas, for instance, a company accused of infringement has only a one-in-six chance of winning at trial. Those odds, plus the threat of an injunction, plus the prospect of spending millions to defend even a small case, made the pressure to settle overwhelming.

To make matters worse, those who had business in court faced a systemic problem that had no malice behind it.

Legal fees increased substantially, in part because of a 1996 Supreme Court decision requiring that trial judges hold focused hearings to determine the limits of litigated patent claims, a process called "claim construction." According to the Court, claim construction is a matter of law-not a factual question that a jury could decide. This means the Federal Circuit can review a trial judge's limit-setting decisions afresh; in fact, patent suits are reversed at a rate of 35 percent and rising. Trial judges trying to avoid reversals reacted by delaying limit-setting rulings. So getting sued for patent infringement meant languishing for 18 months or more before the chance for a summaryjudgment hearing arose.

A Free-for-All Ends

By the late 1990s, patent trolls were finding it easy to attack companies at little risk to themselves. Unlike a company that makes products, a troll faces only the risk of a counterclaim to invalidate the patent it's defending; it's merely a shell that files lawsuits, collects money, and distributes that money to patent owners. Trolls also enjoy a significant cost asymmetry. They have few documents to produce during the documentdiscovery phase of litigation, and much of their legal paperwork can be reused against new defendants in later cases. In many instances, trolls have sued upon patents that are very likely invalid. They then demand settlements, knowing that defending a lawsuit can be more expensive than settling. Many trolls took care to settle before courts could construe the boundaries of the patents in question and issue summary judgments dismissing their cases.

Even some publicly traded companies have covertly been trolling for license fees. Typically, they spin out their questionable patents to shell subsidiaries, which then transfer them to trolls. The public company and the troll have a secret agreement to split licensing fees. The troll is then directed to

seek fees from the established company's competitors. For the public company, it's all risk-free: no counterclaim can be filed against it, and the legal work is done on a contingency basis.

Trolls are choking off economic growth. Small companies cannot afford millions in legal fees, so they pay tribute instead. As the English learned a thousand years ago, however, you can pay *danegeld*, but the Vikings still come back. Large companies can fight trolls, but they risk huge judgments.

Filings of patent suits increased from 2,112 in 1997 to 2,830 in 2006. That does not take into account any increase in the number of defendants per filing. Between 2001 and 2005, the average cost of litigating a large case through trial jumped from \$3 million to \$4.5 million. How much of that jump is due to the increase in filings-and thus in demand for lawyers-is unknown. At several million dollars a case, plus the costs of settlement and of the many expensive patent opinions sought, the direct costs mount. Indirect costs do, too: companies feel obliged to practice "defensive patenting" to protect against infringement claims, and litigation can disrupt a company's operations.

In three quick strokes, the Supreme Court has made things better. Though the recent rulings did not necessarily involve trolls, they will affect them. In eBay v. MercExchange, decided in May 2006, MercExchange sought an injunction shutting down much of eBay's operations. Absent exceptional circumstances, courts used to presume that an injunction should be issued in any instance of patent infringement. But in this case, the Supremes instructed lower courts to apply what's called a traditional test before entering injunctions. The test gives a trial court more discretion to deny injunctions, since the court must assess what is "fair." Trolls can no longer count on getting injunctions, even if they win their cases.

In January 2007, the justices made it harder for trolls to wage licensing cam-

paigns. Before, trolls could send letters to targeted companies, putting them on notice—and in so doing putting them at risk of being found "willful" infringers facing triple damages. Companies that wanted to remove that potential liability, however, could not themselves file suit to get a court to declare that they were not liable. Now, according to *MedImmune v. Genentech*, as interpreted by the Federal Circuit, a company receiving a letter referencing its activities and offering a patent license may file a lawsuit where it resides.

And in April, in KSR International v. Teleflex, the Supreme Court made it easier to find that a patent should not have been issued in the first place, or that it should be declared invalid once sued upon. In KSR, the patentee claimed a patent on the combination of a gas-pedal accelerator and a sensor. The Court found the combination obvious and the patent consequently invalid. The Supremes have reëmphasized that "obvious" inventions are not entitled to patent protection. Districtcourt judges may now use common sense to determine whether a patent for a combination of existing technologies merits protection.

My most cynical Berkeley law professor liked to point out the flaws in the professed values of any legal system. But he once made the enlightened observation that "there is a universal abhorring of waste." It offends everyone's sense of justice when sham plaintiffs shake down hapless victims on meritless claims. We need to cut back on patents that should never have been issued. Injunctions should be used sparingly. Ancient notions of natural law gave rise to equal protection, and forum shopping (filing suits in favorable jurisdictions) threatens that. With its recent decisions, the Supreme Court has put patent law on a sounder footing, to the benefit of us all. TR

Scott Feldmann is a partner in the Irvine, CA, office of the law firm Crowell and Moring.



Optical devices made of silicon

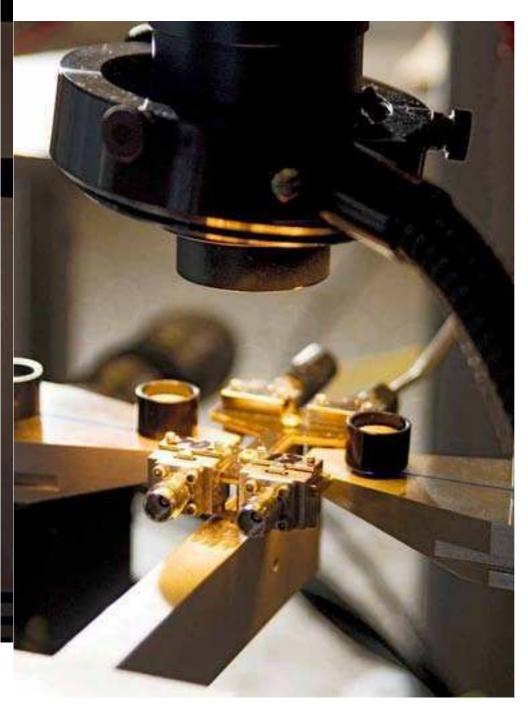
could transform communications networks and computing. By Kate Greene

e're going to be communicating with terabits of information in the next decade," says Mario Paniccia, an Intel fellow and director of the Photonics Technology Lab in Santa Clara, CA. A terabit of data is the capacity of roughly 35 DVDs. But today's fastest telecommunications networks use chips that zip data around at 10 to 40 gigabits per second, and most networks use expensive, clunky components that are assembled piecemeal and achieve lesser speeds. "The ability to have an integrated chip that can transmit and receive a terabit is a compelling solution, and we're still talking a chip the size of your fingernail," says Paniccia, holding in his palm three silicon chips that could prove to be the heart of that solution-thumbnail-size squares that reflect light like mirrors.

Photonic technology, which uses light to transmit data, is the key to networks with terabit-per-second speeds. But silicon, a mainstay of the electronics industry, has been largely useless for photonics because of its poor optical properties. Photonics researchers have had to rely on exotic semiconductors such as indium phosphide, which emit light easily but are expensive and hard to work with. But in 2004, Paniccia's group showed that silicon could be used to make a modulator that encodes data onto a light beam at one gigabit per second. (Telecom companies are beginning to use non-silicon-based modulators that operate at 40 gigabits per second.) Then, in 2005, the Intel researchers bumped up the speed to 10

gigabits per second and built a surprisingly good all-silicon laser (see "Intel's Breakthrough," July 2005).

Intel's goal is to build a single silicon chip that integrates a laser, modulator, and detector, so it can emit light, encode it with data, and register incoming signals. Such a chip, says Paniccia, will affect several areas of technology. It could boost Internet bandwidth, because telecom networks would have access to more and cheaper integrated chips. It could enable new types of optical cables that transfer full-length



movies from computers to iPhones or other mobile Internet devices in seconds. And computers themselves would speed up if the sluggish copper wiring that shuttles data between circuits on a microchip, and between the chip and the computer's memory, were replaced with beams of light.

In building these new optical chips, Intel plans to piggyback on existing silicon fabrication technology such as the lithographic systems used to pattern tiny transistors onto chips. Paniccia says that the ability to build photonic devices on large silicon wafers, using fine-tuned lithography to carve out features, could someday make photonic devices nearly as cheap and abundant as transistors. And if Intel has its way, integrated photonic chips that use silicon-based components will be on the market within the next five years.

ter) leads Intel researchers developing silicon photonic devices. In his hand (left), he holds a test fixture with a modulator mounted at its center, a die holding numerous light detectors, and a gold-colored, fingernail-size square of hybrid lasers, built on a silicon substrate. A microscope is used to set up the modulator tests (right.)

"The Intel group has essentially been debunking the myth that silicon isn't good for photonics," says Alan Willner, a professor of electrical engineering at the University of Southern California.

The Current Work

Researchers in Paniccia's lab are spending a lot of time tweaking the designs of three key silicon-based devices. One, the silicon hybrid laser, was first demonstrated in September 2006. While the all-silicon laser announced in 2005 emits light at near-infrared wavelengths useful for medical applications, the hybrid laser operates in the infrared range used in telecommunications networks. It is this laser that Paniccia calls the "game changer" for telecom and consumer electronics applications.

To make their silicon laser produce light at the right wavelengths, the researchers needed to use a small amount of indium phosphide. The trick was to develop a glue that easily bonded the two materials together. At present, Paniccia's team is trying out slight variations on the design to improve performance. For instance, to reduce power consumption, the researchers are changing the position of the metal contacts that supply electricity to the laser.

The second device the group is working on is the modulator, which enables light to carry data. When laser light enters a conventional modulator, the modulator rapidly turns it on and off, encoding the 1s and 0s of binary data onto the beam. Modulators are usually made of expensive materials, such as lithium niobate, that easily alter light passing through them if a voltage is applied. Since silicon doesn't readily

Demo



NEED FOR SPEED Currently, copper wires transport data between circuits in computer chips. But as the number of processors on the chips increases, copper won't be fast enough. Researchers test a computer motherboard (above) that instead uses photonic devices to move data.

alter light, Paniccia had to turn to a different design, which takes advantage of the material's ability to guide light through channels. His modulator uses an interferometer, a device that creates interference between waves of light. Light enters one end of the modulator and is split into two beams. An electrical device alters each beam's phase—basically, knocking the two light waves out of sync. Then the beams, with their slightly altered phases, recombine. The result is a beam that flickers on and off, representing digital information.

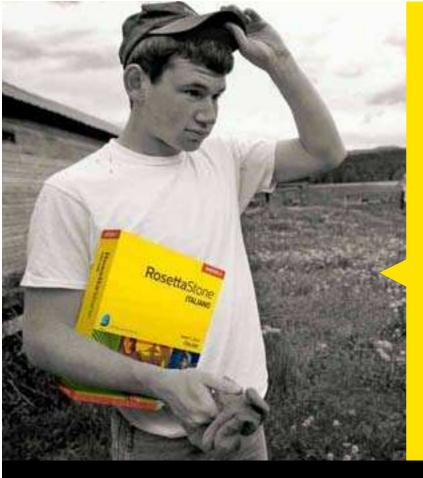
This past July, Paniccia announced that his group had made a silicon modulator that can operate at a recordbreaking 40 gigabits per second—as fast as the best modulators currently used in the telecom industry. There's

still work to be done on the design, to optimize the device's performance. But Paniccia thinks mass production is viable.

The last part of the silicon-photonics puzzle is a working detector that can receive light from a laser and modulator. Again, Paniccia is attempting to overcome a basic limitation of silicon: it doesn't absorb light very efficiently. He and his team have been experimentally adding atoms of germanium to silicon to change its photonic properties so that it can absorb light at telecom wavelengths. They've built detectors that operate at 20 gigabits per second, but that figure is constantly improving as the researchers vary the way the germanium is added and tinker with the design of the electrical contacts. Paniccia expects to have a 40-gigabit-per-second detector operating by the fall.

Paniccia refers to the next stage of development as the "valley of death," because unforeseen problems can crop up as a technology moves from the lab to the market. But he and his coworkers are optimistic. Paniccia points to the guts of a computer that is using a combination of lasers, modulators, and detectors made of traditional optical materials—each device is about the size of a deck of cards and can cost hundreds of dollars—to transfer data around the motherboard. He hopes to replace those devices with photonic chips mass-produced on the same scale as the microprocessors.

If silicon photonic chips are built into computers, says Paniccia, a lot will need to change, including fundamental functions such as the way the computer boots up and the way the microprocessor accesses memory. "No one's looking at these problems yet, because there hasn't been a reason to," he says. But now that the various elements of silicon photonics are becoming a reality, that might be about to change. "Silicon photonics is making us rethink a lot of things," he says.



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NANOTECHNOLOGY

Controlling Color with Magnets

New material can become any visible color

SOURCE: "Highly Tunable Superparamagnetic Colloidal Photonic Crystals"

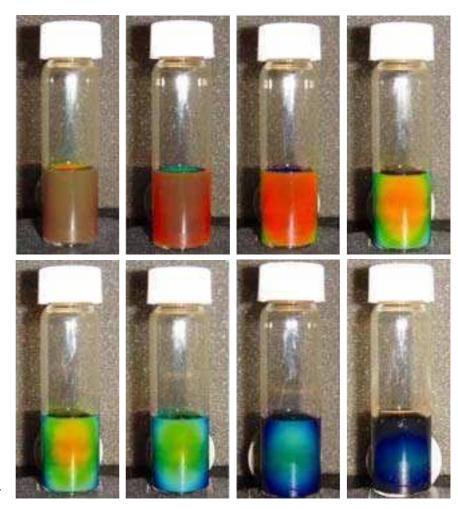
Yadong Yin et al.

Angewandte Chemie International Edition online, July 3, 2007

RESULTS: Researchers at the University of California, Riverside, have demonstrated that a liquid containing suspended magnetite particles changes colors in the presence of an electromagnet. The liquid can be made to reflect any visible color and can switch colors at a rate of twice per second.

WHY IT MATTERS: Others have made magnetically controlled color-changing materials, but the colors covered only small parts of the spectrum, and the materials took longer to switch colors than the Riverside researchers' do. The new materials could be used as sensors that register changes in magnetic fields. And microcapsules full of the liquids could eventually be used as pixels in rewritable posters or other large displays.

METHODS: The researchers used a new high-temperature method to synthesize nanoscale, crystalline magnetite particles, which were then induced to form clusters. The researchers treated the clusters with a surfactant that creates an electric charge on their surfaces. This charge repels neighboring clusters. They then applied a magnetic field, counteracting the repellent forces; the stronger the field is, the closer together the clusters get. As the



A solution of nanoscopic iron oxide particles changes color as a magnet gets closer to it, causing the particles to rearrange. The color changes from red to blue as the magnetic field's strength increases.

clusters rearrange themselves, the solution they're suspended in reflects light of different colors.

NEXT STEPS: The researchers hope to increase switching speeds by confining smaller amounts of material in microscopic spaces. They are also developing applications such as sensors and displays.

Nanowire Microscope

A tiny laser could reveal new details about the structure and behavior of living cells

SOURCE: "Tunable Nanowire Nonlinear **Optical Probe**"

Jan Liphardt, Peidong Yang, et al. Nature 447: 1098-1101

RESULTS: Researchers have developed a nanowire-based laser smaller than a red blood cell. They incorporated the laser into a type of microscope that combines multiple microscopy techniques and achieves a resolution of about 100 nanometers.

WHY IT MATTERS: In addition to imaging by means of light, the microscope could eventually probe cells by applying finely controlled amounts of force with the nanowire; it could then monitor how these forces change the shape of cells and how the cells respond to such mechanical stimuli. This could give researchers a better understanding of how cells work.

METHODS: Tiny forces exerted by light from an infrared laser hold the nanowire in place. The laser also serves as an optical pump, providing a source of energy that induces the nanowire to emit green light. Images can be obtained by measuring the light that either passes through or reflects off a sample as the nanowire moves over it. The device can also be used to trace the shape of a cell membrane by monitoring the displacement of the nanowire as it moves across the membrane.

NEXT STEPS: The researchers will modify the shape of the nanowire so that the laser can better hold it in place: the wire tends to slide around in the optical trap. A conical shape could give the device better resolution and give the researchers increased control over mechanical probing.

BIOTECHNOLOGY

Transplanting a Genome

Scientists successfully transform one bacterial species into another

SOURCE: "Genome Transplantation in Bacteria: Changing One Species to Another"

John I. Glass et al. Science online, June 28, 2007

RESULTS: Scientists at the J. Craig Venter Institute in Rockville, MD, have transferred the entire genome

of one bacterium into another bacterium. The host bacterium took on characteristics of the donor—for example, producing proteins specific to that species.

WHY IT MATTERS: Venter and his colleagues aim to build genomes from scratch and transplant them into bacterial cells in order to create custommade microörganisms, including ones that produce fuel. Successful genome transplant techniques will be necessary to complete this process.



Colonies of successfully transformed bacteria are shown here in blue.

METHODS: The scientists isolated the DNA of one species of mycoplasma, a type of bacterium with a very small genome, and gave it an additional gene to make it resistant to an antibiotic. The DNA was then transplanted into a related mycoplasma species. As the host bacteria grew and divided in the presence of the antibiotic, cells carrying only the species' original chromosomes died, leaving just the cells with the transplanted chromosome.

NEXT STEPS: Venter Institute researchers will next try to determine whether or not genome transplantation is possible in other species of bacteria. They are also developing a synthetic version of the genome of a different species of mycoplasma, which they will attempt to transplant as well.

Genes for Several Common Diseases

A study of seven illnesses, including diabetes and cardiovascular disease, identifies possible culprits

SOURCE: "Genome-Wide Association Study of 14,000 Cases of Seven Common Diseases and 3,000 Shared Controls"

The Wellcome Trust Case Control Consortium Nature 447: 661–678

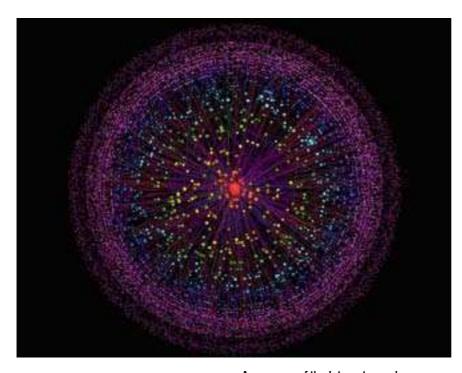
RESULTS: A massive genetic study carried out in the United Kingdom pinpointed 24 genetic markers that increase risk for seven common illnesses. The study found one marker for bipolar disorder, one for coronary-artery disease, nine for Crohn's disease, three for rheumatoid arthritis, seven for type 1 diabetes, and three

for type 2 diabetes.

WHY IT MATTERS: Unlike rare diseases such as Huntington's, where a single genetic variation guarantees that a carrier will be afflicted, common diseases are triggered by a complex array of factors, including multiple genes each exerting a modest effect. The new study illustrates the success of a new approach to gene hunting known as genomewide association, in which scientists scour the entire genome for diseasespecific variations. The vast scope of such studies-in this case, almost 10 billion pieces of DNA-provides enough statistical power for researchers to find genetic variations that raise the risk of disease by a modest amount.

METHODS: The scientists used gene chips to analyze 500,000 genetic markers in each of 17,000 people. To identify genetic variations linked to specific diseases, they compared the DNA of 2,000 patients who had one of the diseases with that of 3,000 healthy controls.

NEXT STEPS: The researchers will try to confirm additional genetic variations hinted at in the current study by analyzing genomic information from larger numbers of people.



INFORMATION TECHNOLOGY

A Better View of the Internet

A new map of the network could help route traffic more efficiently

SOURCE: "A Model of Internet Topology Using K-shell Decomposition"

Shai Carmi et al.

Proceedings of the National Academy of
Sciences 104: 11150–11154

RESULTS: Researchers have developed a new approach to analyzing networks and have used it to create a map of the physical links between Internet service providers (ISPs). The map shows that the Internet consists of a dense core of a few well-connected nodes, surrounded by a large number of nodes that can connect to one another without going through the core and an intermediate number of nodes that link to the rest of the network through the core only.

WHY IT MATTERS: More and more video and other large files are being accessed online, but because of network deficiencies, downloads can still take hours. In today's Internet, data

A new map of the Internet reveals its underlying physical structure.

is mostly routed through major hubs. The researchers' map shows that Internet traffic could be routed around the dense central core to avoid congestion, since even if this core is removed, the majority of ISPs are left connected.

METHODS: The researchers enlisted more than 6,000 online volunteers from about 100 countries, who downloaded a program that traced the routes that data packets took from their computers. The researchers collected up to six million measurements a day over a period of two years, identifying about 20 percent more of the interconnects between ISPs than ever before. To investigate the resulting map, the researchers departed from the usual measure of a node's importance. Instead of simply counting the number of connections, their measure adjusts for the importance of those connections-whether they lead to major hubs or to less connected nodes, for example.

NEXT STEPS: The researchers intend to apply their analysis to other networks, such as human social circles and biological networks that govern intercellular communication.

Keeping Gadgets from Interrupting

Technology detects conversations while maintaining privacy

SOURCE: "Conversation Detection and Speaker Segmentation in Privacy-Sensitive Situated Speech Data"

Tanzeem Choudhury et al. Interspeech 2007, August 27–31, Antwerp, Belgium

RESULTS: Researchers have developed software that can determine when a conversation is occurring and who is speaking. The voice data collected cannot be reconstructed into intelligible speech, so the system maintains a certain level of privacy.

as cell phones become more prevalent, they are constantly interrupting people at inappropriate times. Engineers are interested in building context-aware devices that can determine when it's suitable to notify users that someone is trying to contact them. One approach is to let a gadget with specialized software "listen" to conversations and decide whether it should interrupt.

METHODS: The researchers used a wearable microphone to collect conversation data from a group of 24 people over a span of 4,400 hours. As the audio data was collected, it was immediately processed so that only features such as the presence of speech and its rate, volume, pitch, and tone could be estimated. From such scant data, the verbal content of a conversation can't be reconstructed. To determine who was speaking at any point in the conversation, the researchers used algorithms that looked for changes in these features and pauses in speech.

NEXT STEPS: The researchers plan to analyze more interactions to see how accurately they can determine whether, say, someone is speaking with a boss or a friend.

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Please Don't Give Me a Break!

Max Levchin, cofounder of PayPal, talks about why he needs to keep working. By Michael Patrick Gibson

Shortly after being named the 2002 TR100 Innovator of the Year, Max Levchin left PayPal, the company he had cofounded, which he and his partners sold to eBay for more than \$1.5 billion. About a year later, he founded Slide, a company that creates playful ways to showcase photos on home pages, blogs, and social-networking websites like Facebook. Slide is currently one of the most popular services of its kind, allowing the images of more than 120 million users to swirl, revolve, fade, or "steam" into existence somewhere on Web.

Technology Review: If you were able to give your 26-year-old self any advice, what would you say?

Max Levchin: Don't take the year off between companies.

Why?

It was probably the most miserable year of my life, between PayPal and Slide. If you start companies for fun, you find, unless you're capable of truly relaxing and not thinking about new ideas and work, that it's actually painful to take time off. If somebody told me, "You will go stir-crazy; you won't be able to keep your mind off the markets; you'll keep thinking about stuff, and it'll be more pain than good," I'm not sure I would have listened. But that was a year when I could have done some awesome work. Instead, I was really trying to relax, and that didn't work out at all. Do you find greater fulfillment in pro-

Do you find greater fulfillment in producing rather than—

Consuming? Absolutely. One of the interesting lessons I've learned is that you only value things when

they're scarce. It really extends all the way down to your personal life. And I think if you're an entrepreneur, you're an extreme scarcity fanatic. You're fundamentally trying to find or create things that are scarce and arbitrage that. And so when you have ridiculous and, therefore, worthless amounts of time, you tend not to value it at all. When you work as hard as we do starting companies, you have three hours to sleep and four hours to take off during the weekend. Those are the best four hours you get. You're still thinking about work, but you're very thankful to have that time to ride a bike for a while.

What's your biggest challenge ahead?

On a personal level, a CTO ultimately is still an engineer, which is what I am by training and by first love, and I still love engineering-you feel like you're moving the needle with your own hand. Engineers are happiest when they feel like they're contributing to a cause by doing something. And a lot about being a CEO is learning how to contribute to the cause less by your own hand and more by motivating others and feeling happy when they accomplish goals, sharing in their success and celebrating it and channeling it to others. That's not a particularly engineeringtype thing to do. My biggest challenge is that I'm still learning to delegate. Do you have any advice for this year's

Do you have any advice for this year's members of the TR35?

One piece of advice I sort of wish I had heard is "Do it again. Keep at it." I had considered going off and studying theoretical math for a while, because that's what I really wanted to



do when I was younger, or going to join a more financially bent institution like a hedge fund or a VC. I played around with those ideas in my head and met with people who could give me advice, many of whom were very keen on recruiting me to do those kinds of tasks. And eventually I realized that if you're cut out to be an entrepreneur, you're not going to be particularly happy doing something else. You're only kidding yourself into thinking something else might work. I wish someone had told me at the time of the TR event—

To know thyself?

Yeah, you're exactly who you are; you're going to start another company. The funny thing is that the one thing I was really into before, during, and after PayPal was math and number theory. I really wanted to do a PhD in number theory or cryptography. This may sound a little geeky, but if I had an infinite amount of time and ability to focus on things that aren't business related, it'd be exactly what I'd want to do. One day during my year off, I got to talking with the person that I wanted to be my PhD advisor, who was at first quite keen on this idea. But eventually he said to me, "You know, you're kidding yourself. You're going to go start another company. Just deal with it." And I said, "No, no, come on, Dan, I'm going to make it happen!" And he said, "Nah, you're going to start another company." And he was right. R

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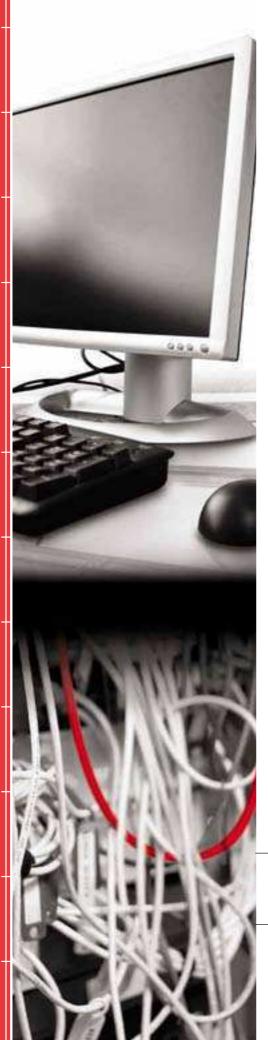
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